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SURGICAL PATHOLOGY

By

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WITH 349 ILLUSTRATIONS
AND 13 COLORED PLATES

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FOREWORD

EACH generation builds from the shoulders of the generation before. The pioneer pathologists of the past generation laid a foundation for the science of pathology which was very important, but their knowledge of pathologic conditions was acquired largely from the postmortem room. Even specimens removed at biopsy were cadaverized before they were submitted to microscopic examination. Today pathology is a science dealing with living things and conditions. It furnishes a groundwork of knowledge which facilitates early diagnosis of disease in the living, and its cure by scientific methods.

What is needed today in the literature of surgical pathology is a work that will serve as a hand book to the surgeon, and the internist, and a guide to the beginner in the field of medicine. Dr. Boyd has made an earnest effort to fill this need. His book is didactic in tone, as is necessary in a volume of this scope, not judicial, fortunately, because to be judicial one must deal only with proved facts and give no play to scientific imagination. It is a sincere attempt to place pathology before the student and the practitioner from the practical standpoint.

WILLIAM J. MAYO.

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PREFACE

The object of this book is to present those aspects of pathology which will prove useful to the surgeon. Modern surgery is based on pathology as much as on anatomy, but the ordinary text-book of pathology contains a large amount of material of little interest to the surgeon, and it often lacks a detailed discussion of the very subjects regarding which he is seeking information. In the present volume an attempt is made to meet this want.

The treatment of the various subjects may appear uneven, but this is because we have tried to maintain a reasonable balance between the common and important conditions and those which are rare and of less importance. To treat every condition at equal length conveys an entirely wrong sense of proportion to the reader. Further information on the more recondite subjects can be found in the references at the end of each chapter.

A list of references may be so long as to defeat its own object, which is not to display the erudition of the writer, but rather to induce the reader to go further afield in his search for knowledge. In preparing the present work the writer has considered that his object would be best served by giving only the most important references, and those mostly in English, except where the information cannot be obtained in that language.

Although not strictly in place in a work on pathology, the clinical features of most of the conditions have been summarized, so that the relation of the pathology to the symptomatology could be demonstrated. The chapter on Surgical Bacteriology is intended to be of use to the surgeon, not to the bacteriologist. It is hoped that the directions for the collection of pathological material, so generally neglected, will prove of value.

The pathological and surgical treatises to which the author is indebted are too numerous for acknowledgement, but he would in particular mention the pathological sections in Keen's Surgery and Ewing's monumental work on Neoplastic Diseases. The basis of the work has been the surgical material examined in the Pathological Department of the Winnipeg General Hospital, the living pathology observed in the operating rooms, and the specimens contained in the Pathological Museum of the University of Manitoba. As far as possible the pathological descriptions have been based upon a study of this material rather than upon the observations of others.

William Boyd.

January, 1925.

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SURGICAL PATHOLOGY

GENERAL PATHOLOGY

CHAPTER I

SURGERY AND PATHOLOGY

"As is our pathology so is our practice." *Osler.*

The surgery of to-day is based on pathology. Unless he builds on that solid foundation the surgeon is no better than a hewer of flesh and a drawer of blood.

It has not always been so. We do not need to look far into the dark backward and abysm of time to realize that the foundation of surgery was the sand of empiricism rather than the bed-rock of pathology. A brief survey of the surgical achievements of the great ones in the history of medicine will show that these, often wonderfully brilliant, lacked the sure basis which could make possible further progress to fresh triumphs, although here and there struggles towards the light can be detected.

Long before the Christian era the Egyptians and many others used to trephine the skull for migraine and epilepsy: a remarkable tour de force, but one which could not be followed up. Hippocrates himself, with all his marvellous powers of observation, with all his clinical acumen and daring as a surgeon—was he not the first to tap the hydrocephalic ventricle?—was grievously handicapped by his ignorance of morbid anatomy.

The great Galen caught a glimpse of the true road to progress and set his foot upon it, for he it was who first introduced experimental methods into medicine, and advocated a consideration of the pathological basis of the disease in determining the appropriate surgical treatment. The man who could observe the effect on the larynx of experimental division of the recurrent laryngeal nerve, who could demonstrate the relation between hemiplegia and hemisection of the spinal cord in a dog, was no mere empiricist. But for more than a thousand years the good seed lay on barren ground, or was choked with weeds.

Even Ambroise Paré, that great clinical surgeon of the 16th century, stumbled upon his method of treating wounds in a purely empirical way. He used to treat gunshot wounds after the manner

of his day by plunging the limb into boiling oil, but on one occasion his supply of oil ran out, and he found to his surprise that the wounds treated with a simple ointment did much better than those to which the orthodox heroic measures had been applied. A great step forward, but certain progress was not possible as long as it was dependent upon such happy chances.

In the history of human progress there appears now and then a thunderbolt, and the thunderbolt of surgery is John Hunter. The history of surgery may without exaggeration be divided into two periods—before Hunter and after. Before him it was content to be an art founded on empiricism; after him it aspired to be a science founded on pathology. He was the first and greatest surgical pathologist. Surgeon, anatomist, physiologist, pathologist, all in one, he towered above his contemporaries like a colossus: From that day the term surgical pathology came to have a real meaning.

It is true that the embryo surgeon of to-day does not always admit that the road to success must lead through the study of pathology. He may be tempted to turn away with a gesture of intellectual fatigue from the tiresome details of morbid anatomy and histology which can only be mastered by years of labor. To learn technic is easy, but to acquire judgment, based so largely as it must be on pathological knowledge, is a very different matter. He who prides himself on being a practical surgeon may be "ever learning, and never able to come to a knowledge of the truth." Such an one is given to peruse the statistics of end results, bristling with sources of fallacy, instead of looking to pathology for guidance in the difficult art of practice. A first-hand knowledge of pathology is the only safe guide for the hands of the surgeon, however skilled those hands may be.

The surgeon himself must be something of a morbid anatomist. He should be absolutely familiar with the gross appearance of diseased tissues. When he operates on a lump in the breast he must be able to say whether the cut surface indicates carcinoma, fibroadenoma, or chronic mastitis. It is an unfortunate tendency of modern medicine to depend too much upon the laboratory, to send the tissue there and await a diagnosis. If a pathologist be available a rapid tissue diagnosis may be made in the course of the operation, but it is even better for the surgeon to be his own pathologist, and to make the diagnosis, as can nearly always be done, from the gross appearance of the tissue.

The microscopic side of pathology also demands attention, and the surgeon can develop a radiographic vision which will pierce through the skin, the deep fascia, the muscles, down to the bones themselves, nay, to the very bone cells which he can watch in his imagination as they marshall their forces, invade the callus, and commence to lay down new bone. Such an one can direct his treatment along rational scientific lines, and need no longer be bound by the shackles of empiricism. That a sound surgical judgment is based on a comprehension of pathological conditions is the first and greatest argument in favor of a study of pathology by the surgeon.

The fundamentals of pathology must be learned in the post-mortem room. There it is that the effects of disease are seen in their nakedness, and mistakes in diagnosis and surgical treatment are laid bare. The disease process can be seen as a whole, and the clinical picture viewed in a way that will often make light the dark places of the case. A tumor of the liver is found to be secondary to cancer in the rectum, the spread of a carcinoma can be traced from the stomach down over the peritoneum to the ovary, an infarct of the lung is seen to be due to thrombosis of the pelvic veins, a cerebral abscess is found to be secondary to an unsuspected bronchiectasis.

The pathology of the past has been built almost entirely on the findings of the post-mortem room, and the medicine and surgery of to-day bear the indelible imprint of that origin. And yet such a method has its shortcomings. The dead-house reveals only the end of the disease process, often only the burnt-out volcano. But surgery is concerned more and more with the beginning rather than the end, for in the beginning there is hope, but in the end too often nothing but despair. To pluck out the weeds of disease they must be recognized in the early stages, else they may so overrun the garden, so deep and branching may become their roots, that eradication is impossible. A breast or a uterus infiltrated with carcinoma, a kidney or a knee joint disintegrated by tuberculosis, are interesting and important objects with whose appearance the student must become familiar. But they convey small hint of the beginning of the process; from them it is difficult or impossible to picture the initial lesion; they are conditions which all can diagnose but for which little can be done.

Moreover many surgical conditions common in everyday practice are but rarely seen on the post-mortem table, for though they may cause much pain and suffering to the patient they seldom result in death, so that statistics compiled from autopsy records may contain grave inaccuracies. The frequency of duodenal ulcer, the appearance of the strawberry gall bladder, the much debated relationship of gastric ulcer to gastric carcinoma and of chronic mastitis to cancer of the breast, the undoubted relationship of tuberculous salpingitis to tuberculous peritonitis, all these we owe to observations made on the operating table rather than in the post-mortem room. Surgery is beginning to repay a little of its debt to pathology.

To the surgeon, then, rather than to the pathologist we are indebted for the conception termed by Moynihan "the pathology of the living," a phrase connoting the study of disease processes as seen in the living body in the operating room. There is, of course, but one pathology, and the expression will not bear too close a scrutiny, but it cannot be denied that a somewhat one-sided view may be acquired from an exclusive study of post-mortem material. A beginning only has been made, but who can doubt that great additions to pathological knowledge will come from the surgeon able to detect the early lesions of tuberculosis of the kidney, sclerosis of the pancreas, and malignant disease of the stomach?

No such contributions, however, are possible without a sound understanding on the part of the surgeon of things pathological. Without that, as Osler says, he will flounder along in an aimless fashion, hitting now the malady and again the patient, he himself not knowing which.

CHAPTER II

SURGICAL BACTERIOLOGY

In this chapter no attempt will be made to give a full description of the bacteria encountered in surgical practice. The intention rather is to present a few points which may be of practical value in the day's work. For a systematic account of the properties of bacteria and the tests employed in bacteriology text-books on that subject must be consulted.

It is often assumed that no bacteriological examination of a case can be undertaken without the assistance of a fully equipped bacteriological laboratory. This is a mistake. The importance of making an ordinary smear on a glass slide from infected material, and staining it with a simple dye such as methylene blue, is not sufficiently recognized. The differentiation between tuberculous caseous material and ordinary pus; the diagnosis of gonorrheal infection, Vincent's angina, cerebrospinal meningitis, and various forms of conjunctivitis; the demonstration of staphylococci, streptococci, Bacillus coli, etc. in pus, can readily be made by this simple method without the assistance of culture media, an incubator, and the other paraphernalia of a laboratory.

Gram's stain is, of course, indispensable for the differentiation of certain organisms. It should always, however, be preceded by the use of a simple dye such as methylene blue. The latter is easier to use, it shows up Gram-negative bacteria more clearly than does the counter-stain used in the Gram method, and it does not give rise to precipitates of stain which may prove confusing and misleading to those not in the habit of constantly employing bacteriological methods. Moreover, if no bacteria be found in the specimen stained with methylene blue nothing is to be gained by proceeding to the use of Gram's stain.

Selective Bacteriostasis.—In connection with the subject of Gram's stain reference may be made to the interesting work of Churchman on selective bacteriostasis. Churchman found that when gentian violet (the active dye in the Gram method) is added to a culture medium it has the effect of preventing the growth of Gram-positive organisms without interfering with that of the Gram-negative group. The growth of the staphylococcus or Bacillus anthracis is completely inhibited whilst Bacillus coli grows freely. This does not mean that the staphylococci are dead; their growth, that is to say their reproduction, is merely prevented, and they may subsequently revive. Churchman therefore uses the term bacteriostasis rather than bactericide.

Acid fuchsin exercises a somewhat similar action. On acid fuchsin agar Bacillus coli grows well but Bacillus anthracis not at all. The flavine dyes, such as neutral acriflavine, behave in the same manner. There is, however, one very important difference between the action of the acid fuchsin and flavine group and the gentian violet group.

If the gentian violet is first added to the bacteria so that the Gram-positive ones are stained and they are now planted on plain agar, the same phenomena will be observed, namely inhibition of the Gram-positive and non-interference with the Gram-negative organisms. The action here is what Churchman terms intrinsic, the dye being given the opportunity of penetrating completely into the bodies of the bacteria. When the dye is in the culture medium, and therefore only comes in contact with the exterior of the bacteria, the action may be called extrinsic. Here the intrinsic and the extrinsic action is the same.

In the case of acid fuchsin and the flavines, however, the two actions are diametrically opposed. The dye exerts one type of selective activity when present in the medium, and an activity of the opposite type when the bacteria are stained with the dye and then planted on plain agar. Bacillus coli grows well on the acid fuchsin agar, Bacillus anthracis not at all. On the other hand when the two organisms are first stained with the dye and then planted on plain agar the process is reversed; the anthrax bacillus now grows well but the growth of the colon bacillus is inhibited.

Caution must therefore be exercised before the results of a test-tube experiment on the bactericidal action of a dye like acriflavine are applied to the treatment of an infected wound, where the conditions are much more akin to those of the dye-containing medium, especially as the dyes are often only used on gauze packed into the wound. The flavines exert a sharp intrinsic effect on the Bacillus coli group as shown in a test-tube experiment, but when the principle is applied to the treatment of wounds it may be found that, although many of the bacteria may be killed by the direct action of the dye, the coliform organisms may persist in the wound which has not been rendered an unsuitable environment for them, whereas the Gram-positive organisms disappear.

This phenomenon of reversed bacteriostasis only holds good for the acid fuchsin and flavine dyes. In the case of gentian violet the intrinsic and extrinsic bacteriostatic actions are parallel and supplement one another, so that it is easier to apply the use of antiseptic dyes to the attack of the Gram-positive than the Gram-negative group of bacteria. The method has already been successfully employed in combating Gram-positive bacteria in infected joints and in wounds.

The intravenous injection of these substances has been employed for attacking both general and local infections. Gentian violet has been used against the staphylococcus, mercurochrome against the colon bacillus, sometimes with brilliant results. The streptococcus, however, appears to defy all such attacks.

The microorganisms of chief importance to the surgeon are: (1) the pyogenic or pus-forming bacteria such as the staphylococcus, streptococcus, pneumococcus, gonococcus, meningococcus, Bacillus coli, and Bacillus pyocyaneus.

(2) Those producing a milder and more chronic type of inflammation, e.g. the tubercle bacillus, the spirocheta pallida, actinomyces, certain of the higher fungi producing such diseases as sporotrichosis and blastomycosis, and the bacillus of glanders. The essential pathological change, at least in the early stage, is the production of granulation tissue, so that these conditions may be grouped together as the infective granulomata, although in some of them suppuration may become a marked feature in the later stages.

(3) A heterogeneous group containing the anthrax bacillus, the tetanus bacillus, etc.

Instead of taking up these organisms one by one, as is done in the ordinary text-books of bacteriology, the needs of the practitioner will be better met by considering the clinical conditions for which they are responsible, and discussing the more important characters of the bacteria in that connection.

INFECTIONS OF THE SKIN

Staphylococci and Streptococci.—Two varieties of infection are met with in the skin, the localized and the diffuse. *Localized inflammation* occurring as a boil, a carbuncle, or an abscess, is generally due to staphylococci; *diffuse inflammation* in the form of a cellulitis is as a rule caused by streptococci. When the abscess is opened the pus should be collected in a sterile tube and sent to the laboratory for examination. In private practice the surgeon may readily examine the pus for himself, for the equipment necessary is of the simplest description, and the technic in no way difficult.

A thin smear is first made on a clean slide, dried, stained with a 1 per cent solution of methylene blue, and examined without a coverglass under the oil immersion lens. If the infecting organism be the staphylococcus it will appear as little groups of spherical cocci, about 1μ in diameter, but in some cases only diplococci may be visible, or the cocci may occur as single individuals. If the streptococcus be present it appears in the form of chains varying greatly in length, the members of a chain often being grouped in pairs. Both the staphylococcus and the streptococcus stain dark blue or black with Gram's stain: they are Gram-positive.

A culture may now be made by smearing a small drop of pus over the surface of an agar slope. It is best to place it in an incubator, but the staphylococcus will grow readily, the streptococcus more feebly, at ordinary room temperature.

The *staphylococcal* growth appears like a thick smear of oil paint, golden yellow, white, or citron colored, according as the strain is S. aureus, S. albus, or S. citreus. The S. aureus is a common cause of local inflammation in skin and in bone. The S. albus is a normal

inhabitant of the skin, and is relatively non-pathogenic, but it may set up pyogenic infection either alone or in conjunction with the S. aureus. It is the common cause of stitch abscesses. S. citreus is rarely present in acute infections.

The staphylococcus produces a powerful proteolytic ferment. which liquefies gelatin and even blood serum, and is responsible for much of the extensive breaking down of tissue seen in these infections.

The staphylococcus is the great cause of localized suppurations. It is found in boils and carbuncles, impetigo and sycosis, acute abscesses, osteomyelitis, and it is one of the most important factors in the production of pyemia.

Resistance to staphylococcal infection is lowered in wasting and cachectic diseases such as diabetes, so that abscesses and boils are common in these conditions. Local infection usually conveys a considerable degree of immunity, and vaccine treatment is often highly successful. A serum has been prepared, but is of no value.

The *streptococcal* culture presents the appearance of numerous, minute, colorless, discrete, semi-translucent colonies, which may easily be entirely overlooked. In fluid medium such as broth long chains are usually formed, but on agar the chains may be either long or short. Speaking generally the long-chained variety is the more pathogenic, the short-chained often leading a saprophytic existence in the body, especially in the mouth and the intestinal tract. This is by no means always the case, however, and it is a mistake to classify the streptococci as St. longus and St. brevis.

There are numerous different strains of streptococci which can be separated by their fermenting action on sugars and their reactions with immune sera, but for practical work they may conveniently be divided into three main groups:

1. St. hemolyticus, producing hemolysis on blood agar, and including the most pathogenic of the strains.

2. St. viridans, producing a green color on blood agar, a normal inhabitant of the mouth, but a common cause of subacute infections, especially of the teeth, the tonsils, and the heart valves.

3. St. mucosus, producing a slimy growth, and surrounded by a well-marked capsule, is more properly classed with the pneumococci. It occurs chiefly in pneumonic exudates and in otitis media, giving the pus a characteristic slimy appearance.

The streptococcus is responsible for a large number of surgical pyogenic infections, usually but by no means always diffuse in character, of which the more important are peritonitis, periostitis and osteomyelitis, otitis media, diffuse cellulitis, circumscribed abscesses, erysipelas, puerperal fever, empyema, and general septicemia. Infection from the streptococcus does not apparently confer any degree of immunity, on account, probably, of the multiplicity of strains. For this reason vaccine treatment is of doubtful value. and antistreptococcus serum of no value whatever.

INFECTION IN THE ABDOMEN

Surgical infections of the abdomen are usually due to the bacillus coli and the streptococcus. The staphylococcus, pneumococcus, Bacillus pyocyaneus, and other organisms may occasionally be encountered.

Bacillus Coli.—The bacillus coli is a short, motile, Gram-negative bacillus, growing readily on agar at room temperature. It is identical in morphological character with the typhoid bacillus, but is readily differentiated from it by the fact that it ferments lactose with the production of acid and gas, whereas the typhoid bacillus has no action on that sugar. Cultures have a characteristic odor suggestive of feces, and in bacillus coli infections this odor may be so distinct as to be of diagnostic significance. It always suggests that the infection originates in the intestinal tract.

B. coli is a normal inhabitant of the lower bowel, and is a common cause of acute suppurative conditions about the intestine, the appendix, the urinary tract, and the gall bladder. It may also set up chronic inflammation of the renal pelvis and the bladder—pyelitis and cystitis —especially in women and children. This latter infection is a very obstinate one, but may sometimes be treated with marked success by means of autogenous vaccines.

In colon infections of the peritoneum the streptococcus is often present as well, although in culture it tends to be swamped by the luxuriant growth of the former organism.

Both come from the bowel, but it is usually impossible to say which is the primary, which the secondary invader. A streptococcal infection of the peritoneum tends to be diffuse and general, a B. coli infection more localized. The pneumococcal form, in which the organisms reach the peritoneum through the Fallopian tubes, is amongst the most serious.

Bacillus Pyocyaneus.—The bacillus pyocyaneus is an organism which is now recognized as a definite disease-producer, and not merely an incidental contamination.

It is a short, small, actively motile, Gram-negative bacillus. Its two most striking characters are its proteolytic power, by means of which it produces liquefaction of gelatin, and its power of producing a green pigment, pyocyanin, which can be extracted by chloroform. Its presence in pus is indicated by a green or blue color.

Although under ordinary circumstances it is hardly if at all pathogenic, yet in conditions of debility it may produce both local and general infections. It delays the healing of wounds, and may cause chronic suppuration in the middle ear, the pleural cavity, the large joints, the gall bladder, and throughout the abdominal cavity.

INFECTION IN THE CHEST

Abscess of the lung and empyema in the majority of cases are due either to the pneumococcus or the streptococcus, the former being the more frequent offender, although during epidemics of influenza

the hemolytic streptococci may attain a position of evil preeminence. The infecting organisms can as a rule be easily demonstrated in smears of the pus, but if few in number culture may be necessary.

Pneumococcus.—The pneumococcus is a small oval coccus, generally occurring in pairs as diplococci, the free ends of which are somewhat pointed, so as to earn the name *diplococcus lanceolatus*. It is surrounded by a capsule, which in ordinary preparations appears as a very characteristic unstained halo. It is Gram-positive. Its appearance in culture is similar to that of the streptococcus, but even more delicate. It is difficult to obtain a pure culture directly from the sputum. The latter should be inoculated under the skin of a mouse; the animal will die within 48 hours of septicemia, the blood containing large numbers of pneumococci. From these a pure culture may readily be obtained.

When injected into animals a powerful agglutinin is produced, which has been utilized for differentiating the various strains of pneumococci, of which at least four are recognized, Types I, II, III, and IV. An efficient therapeutic serum has been prepared against Type I, and has given good results in lobar pneumonia caused by Type I pneumococci.

The *streptococcus mucosus* when tested with antipneumococcal serum shows much more marked agglutination than do the other members of the streptococcal group, and it is now included with the pneumococci.

The pneumococcus is a normal inhabitant of the throat and nose, and its presence is compatible with a state of perfect health. In most cases, however, it is the less pathogenic varieties which are present, namely Types III and IV. When the resistance is lowered owing to such factors as cold or debilitating disease the pneumococcus may become more pathogenic.

In addition to lobar pneumonia and empyema, the pneumococcus may be the casual organism in inflammations and suppurations in almost any part of the body. It may be present in pure culture in pericarditis, peritonitis (especially in children), arthritis, otitis media, meningitis, infection of the frontal and other sinuses, and conjunctivitis. In some cases these conditions occur as a complication of lobar pneumonia, but in others the infection may be a primary one. In the former the infection is carried by the blood stream, and pneumococci can frequently be recovered by blood culture.

INFECTION IN THE URETHRA

Gonococcus.—The gonococcus, the chief cause of acute inflammation in the urethra, first described by Neisser in 1879, is a diplococcus, the adjacent margins of the cocci being slightly concave, so as to present a bean-like appearance. It stains readily with methylene blue, but is Gram-negative, thus resembling the meningococcus and the micrococcus catarrhalis.

Although during the first 24 hours the cocci are extracellular, for ordinary clinical purposes they may be regarded as being typically intracellular during the acute stage of the disease. They are present in large numbers in the polymorphonuclear leucocytes in the urethral discharge, and they are also found in the tissues lining the urethral walls. Late in the disease they may again become largely extracellular.

The organism does not grow at all on ordinary media, and even on solidified human blood-serum it only grows with difficulty at 37° C.

For diagnosis some of the pus may be taken on a swab and smeared on a glass slide, taking care not to pass the swab twice over the same place. Much better results, however, are obtained if a probe or glass rod is used for making the smear rather than a swab. The slide, not the swab, should be sent to the laboratory, as the latter soon dries and becomes useless for the purpose of making a smear. Although the gonococcus is identical morphologically with the meningococcus, no difficulty arises in distinguishing them in practice, for the site of infection is so different.

A useful rule, certainly for all acute cases, is that if one is in doubt about the microscopic picture the case is not gonorrhea. A few doubtful diplococci within the cells together with numerous and varied organisms outside the cells should be regarded as a negative finding. In acute gonorrhea sometimes a few, sometimes many cells are packed with bean-shaped diplococci, and hardly another organism of any kind will be seen between the leucocytes. The pureness of the infection is a valuable aid in the laboratory diagnosis.

The gonococcus may be found in positions other than the urethra. Although easily demonstrated in the vaginal discharge of children, it is extremely difficult to find in the same discharge in adults, being apparently confined to the urethra. It is easily found, however, in smears from the cervix. It may invade the uterus and Fallopian tubes, and is the most frequent cause of salpingitis and sterility in the female. It is a common cause of acute purulent conjunctivitis in infants. In gonorrheal arthritis the organism has been found in the fluid and in the synovial membrane of the joint. It has been isolated from a few cases of gonorrheal endocarditis.

INFECTION OF THE MENINGES

There are four important organisms which may cause meningitis; (1) the meningococcus, (2) the pneumococcus, (3) the streptococcus, and (4) the tubercle bacillus. Of these the commonest is the meningococcus, which will be considered here. The mortality, under efficient treatment, from infection with the meningococcus is about 30 per cent, whereas meningitis due to the other three organisms is nearly always fatal.

Meningococcus.—The meningococcus or diplococcus intracellularis meningitidis of Weichselbaum is an organism which is morphologically identical with the gonococcus, staining readily with aniline dyes, and losing the stain with Gram's method. It grows much more

readily than the gonococcus. It can be cultivated on ordinary agar at 37° C., but grows best on media containing serum.

The meningococcus is present in the cerebrospinal fluid in acute cerebrospinal meningitis, sometimes in large but more often in small numbers. The pneumococcus and the streptococcus, which may produce a very similar clinical and cytological picture, are usually found swarming in the fluid, so that when no organisms can be found the probability is that the infection is a meningococcal one. The distinction is all-important, as there is no condition in which it is so essential to determine the infecting organism. For pneumococcal and streptococcal meningitis there is no treatment and the prognosis is extremely grave: for meningococcal meningitis we have a most efficient serum treatment, and the mortality rate is under 30 per cent. The cocci are generally intracellular but may be extracellular. The typical kidney-shape is readily recognized.

When the organisms are very scanty it is a good plan to place the fluid in the incubator overnight, at the end of which time they may have increased in number.

The meningococcus has the power of fermenting glucose, so that the sugar which is normally present in the spinal fluid is diminished or absent in meningococcus meningitis.

The spinal fluid is almost always turbid, owing to the presence of large numbers of polymorphonuclear leucocytes. During the first few hours of the infection, at which stage lumbar puncture is rarely performed, it may be clear.

INFECTION IN THE EYE

Inflammation whether of the conjunctiva or of the deeper coats of the eye may be produced by a variety of organisms. Acute conjunctivitis may be caused by the ordinary pyogenic bacteria, of which the most important are the pneumococcus and gonococcus—the latter in the gonorrheal ophthalmia of children. Or it may be due to organisms which appear to be specially associated with this region, such as the Koch-Weeks bacillus and the Morax-Axenfeld bacillus.

Koch-Weeks Bacillus.—This is a common cause of acute contagious conjunctivitis. It is a very short minute bacillus, and closely resembles the influenza bacillus in appearance. It is Gram-negative, and is only grown with great difficulty upon serum agar. It is readily demonstrated in smears made from the secretion, and is best stained with weak carbol-fuchsin.

Morax-Axenfeld Bacillus.—This is a short plump diplo-bacillus, very different in appearance from the Koch-Weeks organism, but growing on artificial media with equal difficulty, serum agar being necessary. It is Gram-negative, and stains readily in smears. It produces a subacute form of conjunctivitis, which yields with remarkable readiness to the action of copper sulphate.

Bacillus Xerosis.—The xerosis bacillus is a form of diphtheroid bacillus, closely resembling the diphtheria bacillus morphologically,

and found not only in various inflammations of the eye, but also in the normal conjunctival sac. It can hardly be regarded as a pathogenic organism.

INFECTION IN THE THROAT

Inflammation of the throat and tonsils may be caused by a variety of bacteria, but the principal are the diphtheria bacillus and the streptococcus pyogenes.

Klebs-Löffler Bacillus.—The diphtheria or Klebs-Löffler bacillus is a thin, straight or slightly curved bacillus, about 3μ in length, and either staining uniformly throughout its substance, or showing granules along its course or at the poles which stain of a deeper color. The appearances vary considerably, degeneration and involution forms in which the ends become swollen and club-shaped being frequent.

The bacilli grow readily on ordinary media such as agar, but growth is most abundant and typical on Löffler's blood serum, from which a diagnosis can be made within 12 hours. Not infrequently a direct smear made from the membrane will render an immediate diagnosis possible. When this is done, however, great care should be exercised, for mistakes are much more liable to occur than in the examination of a culture. The arrangement of the bacilli in a stained film is characteristic; they lie scattered about irregularly, often at acute angles to one another, and closely resemble matches spilt out of a box.

The diphtheria bacillus may grow and produce its characteristic lesions in other places than the throat. Amongst these may be mentioned the nose, particularly in children, the ear, and the eye. Many cases of wounds infected with diphtheria bacilli have been reported.

Hofmann's Bacillus.—The pseudo-diphtheria or diphtheroid bacillus, often known as Hofmann's bacillus, sometimes resembles the diphtheria bacillus so closely that it can with difficulty be distinguished from it. It is shorter and thicker than the Klebs-Löffler bacillus, is rarely beaded, is divided transversely by an unstained septum, and tends to be arranged in bundles of parallel bacilli rather than in the spilt match form already referred to. It does not form acid from glucose, and is non-pathogenic to the guinea-pig, whereas the true diphtheria bacillus ferments glucose and kills a guinea-pig in 36 hours.

Hofmann's bacillus is found in many inflammatory conditions in the throat, but it also occurs as a normal inhabitant of many healthy throats. Whether or not it is pathogenic has not been finally determined, but it is certainly not so in any marked degree.

Diphtheroid bacilli have been discovered in every part of the body, and have been accused of causing countless maladies, from general paresis to Hodgkin's disease. If the surgeon receives a report that diphtheroid bacilli have been found in a given lesion, he will as a rule be well advised to attach little weight to such a finding.

Vincent's Angina.—This is a destructive inflammation affecting mainly the tonsils, in which two organisms are invariably found together, a fusiform bacillus and a spirochete.

The *Bacillus fusiformis* is a long, thin, fusiform bacillus, from 10 to 14μ in length, tapering at both ends, and usually showing unstained areas throughout its length. It is Gram-negative, but stains readily with methylene blue. It is strictly anaërobic. For diagnostic purposes a direct smear and *not* a culture is to be made.

The *spirochetes* show several wide irregular curves, and resemble the spirochæta refringens rather than the spirochæta pallida. They stain but faintly with methylene blue, and are best shown by means of weak carbol fuchsin.

These two organisms appear to grow in symbiosis, but it is possible that they may be two forms of the same organism.

INFECTIONS OF THE EAR

The chief bacteria which give rise to inflammation in the middle ear are the streptococcus and pneumococcus, although many other micro-organisms may be found. The streptococcus mucosus, which is now regarded as a variety of pneumococcus, produces a peculiarly slimy exudate. Diphtheroid (Hofmann's) bacilli are often present in the pus, but it is doubtful to what extent they act as a causal agent. Tuberculous infection of the middle ear with resulting caries of the bone is not uncommon in children, and the bacilli may be found in smears of the discharge.

ANAËROBIC INFECTIONS

The anaërobic bacteria are of interest to the surgeon on account of the results which may follow wound infection, results which are extremely common in military surgery, but fortunately rare in civil practice. They are all of fecal origin, and are found both in the feces of man and in manured soil.

The *tetanus bacillus* will be considered in a separate chapter, and need not detain us here.

The most important of the other anaërobes infecting wounds are (1) the bacillus welchii, (2) the bacillus of malignant edema, (3) the bacillus edematiens, and (4) the bacillus sporogenes.

These are all strictly anaërobic. The first three differ from the fourth in one important characteristic. The former are saccharolytic; they have the power of breaking up sugars but not proteins. They are, therefore, not putrefactive in the true sense of the word, and although the odor produced is heavy and disagreeable it is not putrid. The bacillus sporogenes, on the other hand, possesses strong proteolytic powers, and speedily produces a condition of putrefaction, which heralds its arrival by the characteristic putrid smell. It may therefore be said that in the early spreading stage of gas infections it is the saccharolytic organisms which are predominant; it is they which produce the gas. In the later stages the proteolytic bacteria, in themselves nonpathogenic, are enabled to invade the necrosed muscle and induce a state of putrefaction. The clinical changes produced by these bacteria are considered more fully in the chapter on Gangrene (page 74).

It would be out of place to give a full description of the characters of these organisms. Suffice it to say that all are thick, Gram-positive bacteria, but in old cultures many of the individuals may be Gram-negative.

The *Bacillus welchii* is the chief gas producer. It is responsible for the development of gas sometimes seen in the organs at autopsy, and it is the principal miscreant in true cases of gas gangrene. Except when grown in special media it does not form spores. In the tissue fluids it usually has a distinct capsule, hence its name Bacillus aerogenes capsulatus.

The *Bacillus of malignant edema* may be distinguished from the bacillus welchii by the presence of a large central spore. It is the second most frequent organism found in gas infections, and is often associated with the bacillus welchii. It is responsible for the rapidly spreading edema, rather than for the gas.

The *Bacillus edematiens* closely resembles the bacillus of malignant edema both in its morphological characteristics and in its pathogenic properties.

The *Bacillus sporogenes* is a large bacillus, resembling the bacillus welchii, but characterized by the possession of a subterminal spore. Moreover it is actively motile, whereas the other members of the group are either feebly motile (bacillus of malignant edema) or non-motile (bacillus welchii).

These various bacteria are often found together in the same infected wound.

Hospital Wound Infections.—Occasionally, although happily rarely, it happens that a series of operation wound infections appears in a hospital for a period which, although brief in time, may appear long enough to those who have to work under these trying conditions. These infections are usually due to the group of anerobic bacteria under consideration. As they all possess the power, under certain conditions, of spore formation, they are particularly difficult to destroy. Sometimes it is possible to lay one's finger on the *fons et origo mali*, but sometimes this cannot be done.

The cat-gut is always blamed—usually without cause. As a rule it will be found that there is some flaw in the sterilizing procedure, and it is well to look particularly to the gauze and the dusting powder.

These infections usually only follow abdominal operations, especially those on the alimentary canal. They commence in the abdominal wall in the neighborhood of the wound in the intestinal tract. They are rarely met with in operations on the extremities. These facts are interesting in view of the occurrence of the anerobic bacilli as normal inhabitants of the alimentary canal.

VACCINES

Vaccine treatment is a valuable aid in a few surgical conditions. Remarkable, however, as are the triumphs of vaccine therapy in the prevention of disease, it cannot be said that the high hopes at one time

entertained for it as a means of cure have been realized. The craze for vaccines on the part of the profession has been a remarkable example of a lack of the faculty of scientific discrimination. The fallacy of post hoc ergo propter hoc has nowhere received a more striking illustration. Occasionally brilliant results attend their use, but on the whole it must be admitted that they have been relegated to a subsidiary position in the surgeon's armamentarium.

A vaccine is not a cure-all and an end-all. It is merely one factor which may be employed to turn the tide of battle, occasionally with success, against the enemy.

The sphere of vaccine treatment was formerly much wider than it is to-day. At one time it was considered that general infections such as septicemia could be benefitted by vaccine treatment. Such is not the case. The body is already overwhelmed by the bacterial invasion, and any fresh access of organisms is far more likely to do harm than good. The method should be reserved for local infections.

The recent work of Dreyer may prove to be of such importance as to revolutionize our ideas with regard to vaccines. Dreyer points out that, in general, the successes of bacterial therapy and prophylaxis are obtained with microorganisms of the non-acid-fast and Gram-negative varieties. It is to infection by such organisms as the typhoid bacillus that the tissues respond best by the production in large amount of specific antibodies. The failure of the Gram-positive and acid-fast bacteria to stimulate the body to an immunity response is due to the presence of the protective fatty substances referred to on page 93. These bacteria are not readily digested by trypsin, in distinction to the case with which the Gram-negative organisms are broken down. The same appears to hold with regard to the digestive action of the tissue juices, so that the specific bacterial proteins, which are the essential stimulus in the production of immunity, fail to be liberated from the Gram-positive group. Dreyer has been able to remove these fatty substances, and the "defatted" vaccine is of course Gram-negative.

By growing anthrax bacilli and staphylococci at 42° C. instead of 37° C. he changed the bacteria from Gram-positive to Gram-negative, and the fatty content was correspondingly diminished. From this it might appear that the more favorable the conditions of growth, the greater is the production of the protective fatty sheath, so that bacteria growing in the body should be much less fitted to act as an efficient antigen than those grown on artificial media. This would explain the fact, hitherto so difficult to account for, that the additional injection of a few million microorganisms (as a vaccine) in a patient who is already harboring countless billions may prove of great benefit; the vaccine provides the tissues with bacteria which are more readily soluble and thus of higher antigenic value.

Vaccines may be *stock* or *autogenous*. The polyvalent stock vaccine has been mercilessly exploited by the commercial drug houses, greatly to the detriment of vaccine therapy in general. So many strains or varieties of bacteria are contained in these vaccines, that the therapeu-

tic effect of the particular germ which may be causing the infection is reduced to a useless minimum. Such shot-gun methods deserve nothing but condemnation. Any effect which may be produced is due to the action of the foreign protein of the bacteria, and is entirely non-specific in nature.

The importance of care in *collection of material* for a vaccine is usually greatly underestimated. Unless care is taken to prevent contamination, the efforts of the bacteriologist are of no avail. Urine must be collected in a sterile bottle by means of a catheter, and examined at once. The skin surrounding a wound must be sterilized to prevent contamination with the staphylococcus albus. A nasal swab must be taken through a sterile speculum after the nares have been swabbed with a disinfectant. The same is even more true of the collection of material from the interior of the uterus. These all-important matters must not be left to the care of an uninstructed nurse.

Staphylococcal Infections.—It is in staphylococcal infections of the skin that some of the most gratifying results of vaccine treatment have been obtained. Boils are usually caused by the staphylococcus aureus or the staphylococcus albus. An autogenous vaccine should be used, commencing with 200 millions, and going up to 1000 or 2000 millions. A stock vaccine will sometimes give good results.

Streptococcal Infections.—A stock vaccine should never be used, owing to the multiplicity of strains of the streptococcus. It is seldom that even an autogenous vaccine is of any value in surgical conditions. It should never be used in cases of septicemia. The dose is very much smaller than in the case of the staphylococcus; not more than 5 or 10 millions should be given as an initial dose, and 50 millions should be the maximum. Streptococcal vaccines are not of the slightest use in erysipelas.

Bacillus Coli.—Vaccine treatment has a distinct place in B. coli infections of the bladder. It is, of course, essential first to remove any removable cause such as a stone or an enlarged prostate. If the bladder is being continually reinfected by streams of colon bacilli from the renal pelvis the best results cannot be expected. Finally, in every case tuberculosis of the bladder must first be excluded. When, however, an overdistended but otherwise healthy bladder has become the seat of a B. coli cystitis, very satisfactory results may be obtained by means of an autogenous vaccine. Stock vaccines are useless. Moreover, even an autogenous vaccine should be made up afresh every three months, for the organisms adapt themselves to the antibodies which they evoke. The initial dose should not be larger than 50 millions.

Gonococcal Infections.—Gonococcal vaccines used to be employed to a considerable extent in both acute and chronic gonorrhea. They are of no value in either condition. Some cases of gonorrheal arthritis have been greatly benefited by a series of injections of gonococcal vaccine, but the result is in no way a tribute to the specific

effect of the vaccine, for equally good results may be obtained by the use of any foreign protein, such as typhoid vaccine or sterile milk. To obtain the best results the protein must be given intravenously.

Non-specific Therapy.—The basic idea of scientific vaccine therapy is specificity. The bacteria causing the infection are those employed in the vaccine. It has been found, however, that remarkable results may be obtained by the intravenous injection of any foreign protein such as a bacterial vaccine, egg albumen, milk, or albumose. After such an injection the patient develops a severe rigor, the temperature rises to 103° or 104°, there is a well-marked leucocytosis, and ferments and antiferments appear in the blood. As a result of these phenomena, although by what exact mechanism we are still in the dark, certain chronic infections, particularly cases of chronic arthritis, may suddenly show most marked improvement. A striking example of such a case is given on page 765. The non-specific reaction bears many points of resemblance to anaphylactic shock, and anaphylactic conditions such as asthma and urticaria may derive marked benefit from this method of treatment.

I have found that the cases which respond best are those which manifest signs of chronic intoxication such as malaise, occasional slight rise of temperature, palpitation, tachycardia, a muddy complexion, etc. I have not found it possible, however, to predict with any certainty in which cases a favorable result may be expected. The commercial typhoid vaccine is a convenient foreign protein to use. It must be diluted so that 1 c.c. contains 100 million bacteria. The initial dose (intravenous) should not be more than 0.25 c.c. and 1 c.c. is sufficient for a maxium dose. The method is not without risk, and must never be employed in patients with heart disease. Peptone solution, carefully prepared and neutralized, has the advantage that its use is unattended by many of the unpleasant toxic effects of typhoid vaccine injections, such as rigors and malaise. It is given in the same way, commencing with 0.3 c.c. and reaching a maximum of 1.3 c.c.

Tuberculin.—Tuberculin may be regarded as a special variety of vaccine. A full consideration of the various forms of tuberculin would be out of place here. Suffice it to say that they contain in varying degree the toxic substances of the tubercle bacillus.

Tuberculin may be used for two purposes, diagnostic and therapeutic. It is essential to realize that the dosage is entirely different in the two cases. Koch's Old Tuberculin may be taken as an example. One cubic centimeter contains one gram or 1000 milligrams. The *diagnostic* dose is 0.5 mgrms. The tuberculin has therefore to be diluted so that 1 c.c. = 1 mgrm., and of this 0.5 c.c. is injected subcutaneously. The patient is kept in bed, and a rise of temperature of more than one degree during the next 12 hours indicates a positive general reaction. A focal reaction may also occur. In one case in which I used the method for determining the nature of a chronic iritis there was so marked a reaction in a scar at the site of a previous operation for tuberculous glands in the neck that the red wheal could be

seen from the other side of the ward. The reaction in the eye, however, was in no way alarming.

The subcutaneous method is far the best for purposes of diagnosis. The cutaneous method of *Von Pirquet*, however, is so widely employed that reference must be made to it. A drop of Old Tuberculin is placed on the arm and the skin scarified through it. A control test with no tuberculin must always be made. A raised reddened area of more than 5 m.m. in diameter indicates a positive result. Except in young children the test is positive in such a large percentage of persons, altogether apart from the question of whether they are suffering from active tuberculosis, that it is of little diagnostic value. It indicates tuberculous infection, not tuberculous disease. A negative result is of some value, a positive result of none.

When used *therapeutically* in a series of injections the dose must be infinitely smaller. The initial dose should not be more than $\frac{1}{10{,}000}$ mgrm., and only by slow degrees should it be increased. Koch's New Tuberculin, which contains more of the actual substance of triturated tubercle bacilli, should be employed.

It appears possible that the whole of our ideas regarding tuberculin will be revolutionized by Dreyer's work (vide page 32 and 93). By removing the fatty envelope from the tubercle bacillus and thus converting it into a non-acid-fast organism he has enormously increased its antigenic power. Only the preliminary observations have been published, but of the four guinea pigs with active tuberculosis treated with "defatted" tuberculous antigen all four recovered. The organs of one pig, which subsequently died of another condition, showed healed tuberculous lesions.

Coley's Fluid.—It has been known for a considerable time that malignant growths may occasionally disappear after an attack of erysipelas. Later it was found that when Bacillus prodigiosus was grown in company with the streptococci of erysipelas the virulence of the latter was increased. Coley's fluid consists of the mixed toxins of these two cultures.

A marked febrile reaction is produced by the injection, and it is undoubtedly true that many cases of sarcoma of all kinds, with the exception of the melanotic variety, have disappeared as a result of the treatment. The sarcoma becomes soft, caseous, and finally breaks down and liquefies, or undergoes absorption. The same good results are not obtained in carcinoma, nor, it may be added, are they usually obtained in the hands of other surgeons than the originator of the method. Coley's own results, representing work commenced in 1892 and carried down to the present day, are in many ways remarkably encouraging.

SERA

Diphtheria antitoxin is one of the greatest gifts of bacteriology to medical science. The very greatness of its triumph has led to

the vain hope that efficient sera can be manufactured against many of the other pathogenic bacteria. Valuable sera have been prepared against tetanus, cerebrospinal meningitis, poliomyelitis, pneumonia due to Type I pneumococcus, anthrax, and (possibly) gas gangrene.

Tetanus.—It is as a *prophylactic* given shortly after the receipt of a wound that tetanus antitoxin has its greatest value, a value which was abundantly proved on a gigantic scale during the war, In every case in which an open wound is accompanied by laceration or crushing of the tissues, or is grossly contaminated by garden soil or city dirt, an intramuscular injection of 1000 units of antitoxin should be given to an adult, 500 units to a child. Some authorities consider that these doses are unnecessarily large, and doubtless 500 units would be a quite efficient prophylactic for an adult. The prophylactic dose may be followed by the appearance of a local tetanus. The antitoxin is unable to neutralize that portion of the toxin which is already creeping up the motor nerves from the wounded part to the cord, and which may lead to the development of local symptoms, but it completely destroys the large amount of toxin which enters the blood stream, and which, being carried to all parts of the body, would be absorbed by innumerable motor-end plates and pass along the corresponding motor nerves to the spinal cord. It is evident, therefore, that everything depends on the promptness with which the prophylactic injection is given.

Its value as a *therapeutic agent* is, unfortunately, very much less, for it cannot dislodge any toxin which has once become anchored to the nerve cells. At the same time it can at least prevent the fixation of further toxin to the cells, and some of those best fitted to judge consider that the experience in the war amply supports the intraspinal injection of serum. Bruce's work in this respect is particularly noteworthy. Describing some experiments on monkeys by Sherrington he remarks that in the cases treated by intramuscular injections the disease was hardly retarded in its fatal result, whereas almost all those treated by the intrathecal route recovered. "The proof of the pudding is in the eating of it. Treated intramuscularly they all die. Treated intrathecally the great majority live." In one series of 200 cases of war tetanus Bruce records a mortality of 36.5 per cent; in a later series of 100 cases treated intrathecally the mortality was 19 per cent. Rather more than 20 c.c. of cerebrospinal fluid should be withdrawn under a general anesthetic, followed by the intrathecal injection of 20 c.c. of high potency serum containing 16,000 units. At the same time an intramuscular injection of 8000 units should be given. These large doses should be given once a day for the first two days, and they may then be cut down by half. At the second injection the cerebrospinal fluid may be found to be purulent, owing to the irritation produced by the serum, but it remains sterile.

Cerebrospinal Meningitis.—Antimeningococcal serum, introduced by Simon Flexner, differs from diphtheria and tetanus antitoxin in that it exerts its action against the infecting bacteria, and not against

their toxins, which are not given off as exotoxins. By the early use of this serum the mortality has been reduced from 80 per cent to 30 per cent or lower.

In an adult from 30 to 60 c.c. may be given, depending upon the severity of the infection, but in no case must more serum be given than the amount of cerebrospinal fluid which can be withdrawn. In children from 10 to 20 c.c. is sufficient, but rather more than that amount of spinal fluid should be drawn off. The injection should be repeated every day until meningococci disappear from the cerebrospinal fluid.

In the early stages of the disease the meningococci circulate in the blood, so that at that stage it is good practice to give in addition an intravenous injection. By the time the meningitic symptoms are well developed, however, there is no advantage in the intravenous route, as the bacteria have forsaken the blood for the meninges.

Poliomyelitis.—An acute attack of anterior poliomyelitis confers an enduring immunity both in man and in the experimentally infected monkey. Moreover the serum of the patient continues to contain substances which have the power of neutralising the virus of the disease. Such a serum may therefore be employed for treating early cases of the disease.

The serum has been used as long as 30 years after the original attack, but it is preferable that the time interval should be as short as possible. In an adult donor 500 c.c. of blood may be withdrawn, in a child of 10 years about 200 c.c. The blood is allowed to clot, and the serum is separated, inactivated at 55° C. for one hour, tested for sterility, and put up in sterile bottles. As much cerebrospinal fluid as possible is withdrawn from the patient, and 10 c.c. less than that amount of serum is run in by gravity. It is only during the early febrile period that the treatment is of any value.

COLLECTION OF MATERIAL

In bacteriological diagnosis very much depends on the manner with which the material is collected. Unless this be done correctly the pathologist's report is of no value.

Pus.—Pus may be collected in a sterile tube if there is enough of it. Often, however, it will have to be taken upon a swab. If this has to be sent some distance to a laboratory there is great danger of it drying up.

In certain cases a smear on a glass slide must be made instead of a culture. This must be done in all gonococcal infections, and in looking for the organisms of Vincent's angina.

When a culture is required it should be made by the surgeon at the time the swab is taken, the appropriate medium being used—agar for ordinary purposes, blood serum for diphtheria, pneumococci and streptococci. The tube may then be sent to the laboratory without any fear of the pus drying up.

Blood Culture.—A culture of the blood affords valuable information in various forms of septicemia, such as puerperal septicemia, ulcerative endocarditis, pneumonia, typhoid fever, etc. The blood must

be collected with strict aseptic precautions. It will be found that the more rigid the technic the fewer will be the number of positive results.

The medium used depends upon the organism supposed to be present. For ordinary work broth is suitable, but it must be in sufficient quantity to dilute the blood at least twenty times in order to obviate the antibacterial properties of shed blood and to prevent coagulation. The arm must be thoroughly sterilized either with a 1 in 1000 corrosive sublimate soak for half an hour or by painting with a strong tincture of iodine. From 5 to 10 c.c. are removed from the median basilic vein by means of a sterile syringe and distributed amongst the tubes of broth. If the material has to be sent by mail it is convenient to mix the blood with melted gelatine which is then allowed to solidify. In typhoid cases sterile ox bile should be used, and as this acts as an anticoagulant the blood need not be diluted more than 1 in 3.

One of the most convenient methods of collecting blood for culture is by means of the modified Keidel vacuum tube. The tube already contains the broth, and as the blood is drawn directly into it, the chances of contamination are reduced to a minimum.

Blood for Wassermann Test.—Many unreliable reports on the result of the Wassermann reaction are really due to lack of attention to detail in the collection of the blood. The blood is obtained from any convenient vein, usually that at the elbow, either by means of a syringe or by allowing the blood to flow from a needle into a sterile tube. It is essential that the syringe, needle, and tube contain no water, otherwise hemolysis will occur and the specimen will be spoiled.

The blood should be collected to the amount of at least 5 c.c. in a test-tube, and allowed to stand overnight until the serum has separated from the clot. The clear serum is then decanted into a small sterile tube which is corked and sent to the laboratory. The serum must not be left lying about a warm room, otherwise it may become anti-complementary and give a false positive result. When the blood is to be sent by mail it is always the serum, never the whole blood, which should be dispatched to the laboratory.

In *children* under the age of 18 months, in whom it would be extremely difficult to draw blood from one of the ordinary veins, an abundant supply may readily be obtained by using the superior longitudinal sinus. An ordinary Wassermann needle is attached to a 5 c.c. syringe, and the fontanelle is pierced in the middle line. The needle must be held in an almost horizontal position, as the sinus lies immediately under the coverings of the fontanelle. When the needle is in correct position the syringe is readily filled with blood. The appearance of cerebrospinal fluid in the syringe indicates that the needle has gone too far. There is practically no danger of damaging the brain. Arsphenamin and antitoxic sera can be very conveniently administered to young children by this route.

When the fontanelle has already closed two other methods are available. The blood may be obtained from the external jugular vein,

which stands out prominently when the child cries, and which, of course, must be fixed with the finger. Or we may employ Blackfan's method, which consists in scarifying the skin of the back with a scalpel, and, by means of a suction apparatus such as is used for wet cupping, drawing the blood into a test tube. In this way from 2 to 4 c.c. of blood may be obtained.

Blood for Blood Chemistry.—Blood chemistry estimations for sugar, urea, creatinin, cholesterin, etc. are made on the whole blood, so it is necessary to prevent coagulation. The blood should therefore be collected in a bottle or test tube containing a few drops of 20 per cent potassium oxalate or a few crystals of sodium citrate. Not more than 1 drop of the oxalate solution should be used for each 5 c.c. of blood, else it will interfere with the creatinine estimation. The drop should be evaporated to dryness, leaving a deposit of the salt in the tube. For a single estimation 5 c.c. is usually sufficient, but for a full chemical analysis at least 15 c.c. should be collected. If the blood has to be kept for any length of time before being examined, 1 drop of pure formalin to each 5 c.c. of blood will preserve it, but this must not be used when a urea estimation is wanted, as the formalin would completely interfere with the action of the urease ferment.

Blood for Widal Test.—The serum and not the whole blood is required. The serum, however, can be separated when the specimen reaches the laboratory. It is sufficient, therefore, to collect the blood in a capillary tube or in a Wright capsule. A capillary tube can readily be manufactured by drawing out a piece of thin glass tubing either in a Bunsen flame or even in the flame of a spirit lamp. When one end of such a tube is applied to a drop of blood, the blood will at once flow into the tube. It will only continue to do so as long as air is free to escape at the other end. If the first drop is allowed to flow into the far end of the tube, and thus block the egress of air, no more blood can be obtained. It is best, therefore, to hold the tube either horizontally or slightly inclined upward.

In order to close the tube, gently heat the empty portion of the tube in the flame of a match, and then seal the far end in the same flame. The heated air in the tube will contract on cooling, and thus draw the blood into the center of the tube, holding it firmly there, and effectually preventing its escape. The near end of the tube does not require to be sealed.

Blood for Blood Transfusion Tests.—To *group* a specimen of blood only the corpuscles are required, provided that one has known sera of Groups II and III (see page 43). Two drops of blood are collected in 1 c.c. of normal saline containing 2 per cent sodium citrate. If serum is required for *matching* the two bloods, it is collected as for the Widal test.

Cerebrospinal Fluid.—Lumbar puncture is not a difficult operation except in the case of a very fat subject, but it requires a little practice. The best space to enter is that between the fourth and fifth lumbar vertebræ, which lies just below a line drawn between the highest points

on the iliac crests. The landmarks may conveniently be outlined with iodine.

The skin is sterilized and frozen, or in very sensitive patients a preliminary injection of novocaine may be given; a finger is placed on the spine of the 4th lumbar vertebra; the patient, reclining on one side, is directed to bend his back and draw up his knees so as to widen the intervertebral space, a long needle is inserted a little below and a little to one side of the spine, and pushed forwards, inwards, and a little upwards until the resistance of the ligamenta subflava is passed. If no fluid issues from the needle a stilette should be inserted. If still no fluid appears, and one is certain that the needle is in the canal it is best to try again at a higher level. If a bacteriological examination is to be made the needle must be held in a piece of sterile gauze. The fluid should be collected in two tubes, in order that the source of any blood present may be determined. (See page 640.)

Serum from Chancre.—An examination of the serum from a primary syphilitic sore is of the greatest value for the early diagnosis of the disease. It may be examined in two ways: (1) the dark field method for spirochetes, and (2) the local Wassermann reaction. The *dark field method* is the best and most certain of all the methods of diagnosing syphilis, but its scope is limited, and the serum must be examined for motile spirochetes not more than a few hours after removal from the body. The *local Wassermann reaction* may be performed on serum which has been mailed from a distance. The method of collecting the serum is the same in both cases. The primary sore is sponged with normal saline solution, dried, and gently squeezed. The serum which exudes is collected in as large amount as possible in a capillary tube, both ends of which are sealed in the flame of a match, great care being taken not to heat the serum. In the case of the dark field method trauma must be avoided, as the presence of blood is very undesirable. This is not so important in the case of the local Wassermann test.

Surgical or Autopsy Material.—Specimens intended for histological examination should be cut into small slices, and placed at once in a 5 per cent solution of formalin, in which they may be preserved indefinitely. The tissue should not be placed in alcohol, as this interferes with a rapid diagnosis by means of a frozen section. If a bacteriological examination is desired the tissue should be placed in a dry sterile bottle or wrapped in sterile gauze, and delivered into the pathologist's hands with as little delay as possible. Undue drying makes it unfit for examination.

Urine.—The urine should be as fresh as possible. If a quantitative estimation of any constituent is to be made, it is absolutely essential that a mixed sample of a 24 hours specimen be obtained. In case the urine has to be sent by mail, it is well to add some volatile preservative such as chloroform, as casts may disappear with considerable rapidity in warm weather. Specimens intended for bacteriological

examination must be obtained by catheter, and should be examined as soon as possible.

LEUCOCYTOSIS

The behavior of the leucocytes is of great importance in the diagnosis and prognosis of surgical cases.

But what constitutes a leucocytosis? This question cannot be answered in a word. A count of 10,000 may in general be taken as the upper limit of the normal. In some people the normal count varies between 10,000 and 12,000. On the other hand in certain diseases such as typhoid and influenza the count is much below the normal, so that a rise to the normal may indicate a leucocytosis. Emerson instances a case of typhoid fever in which the count was 1600; a parotitis developed, and the leucocytes at once rose to 3200, a true leucocytosis for the patient at that particular time. Thus the progress of the leucocyte count is of more value in diagnosis, and particularly in prognosis, than one individual count.

Theoretically the total number of leucocytes may be increased owing to an increase in the number of any of the various forms. The large mononuclears are increased in malaria. The lymphocytes are increased in whooping cough, exophthalmic goitre, and in a number of diseases of childhood such as rickets and congenital syphilis. It is important to distinguish between an absolute increase and a relative increase in the lymphocytes. If the polymorphonuclears are decreased there will be an apparent but only relative increase in the lymphocytes, as is seen in typhoid fever and pernicious anemia. In health the total number of lymphocytes varies from 1000 to 3000 per c.mm., the percentage being 20 to 30 per cent.

For practical purposes any marked increase in the number of leucocytes (apart from the various forms of leukemia) may be regarded as being due to an increase in the polymorphonuclears. They constitute from 60 to 75 per cent of the leucocytes, or 3500 to 7500 per c.mm. They are increased in all local suppurations, and in most infectious diseases except typhoid fever, influenza, measles, and tuberculosis, which are usually accompanied by leucopenia. More depends on the organ involved than on the infecting bacteria. Typhoid infection of the lymphoid apparatus is accompanied by a leucopenia, but invasion of the pleura or the periosteum is promptly signalized by the appearance of a leucocytosis. The normal leucocyte count of tuberculosis of the lymph glands is replaced by the high count characteristic of tuberculous meningitis.

The leucocyte count depends on two factors, the severity of the infection and the resistance of the patient. A well-marked leucocytosis of 20,000 or 30,000 is of good prognostic import, since it indicates a good resistance. A slight increase may indicate a mild infection or a resistance which has been overwhelmed by a very severe infection.

These two factors may be separated by means of the differential count. The percentage of polymorphonuclears indicates the severity

of the infection, whereas the total count is an index of the patient's resistance. Thus if the percentage count is much increased in proportion to the total count the prognosis is bad, owing either to severe infection or low resistance.

A study of the leucocyte counts on several occasions may furnish information of great value. An increasing leucocytosis, however low the count may be, indicates a spreading infection, and in the case of appendicitis is an indication for operation.

A *post-digestion leucocytosis* occurs in a person who, having fasted for 12 hours, takes a meal rich in protein. The increase begins in one hour and reaches its maximum in from 3 to 5 hours. The count usually rises to about one third above the normal. The phenomenon is probably related to the leucocytosis which follows an intravenous injection of foreign protein.

During the last months of *pregnancy* there is a leucocytosis in about 75 per cent of women. This is most marked in primiparæ, in whom the count averages about 13,000.

In the *new-born* there is always a high leucocyte count, about 26,000 on the first day, falling to 15,000 on the eleventh day. This high count may be maintained from the third to the sixth year. The differential count in these early years is quite abnormal, for the small lymphocytes constitute from 40 to 60 per cent of the total, and the polymorphonuclears may be as low as 30 or even 20 per cent.

Leucocytosis following internal hemorrhage is a very important variety of leucocytosis, for it occurs in conditions which may readily be mistaken for acute sepsis. It has long been known that hemorrhage into a serous cavity may be marked by a considerable leucocytosis. Subdural hemorrhage from fracture of the base of the skull, pachymeningitis hemorrhagica interna, ruptured ectopic gestation, and other examples of internal hemorrhage may be accompanied by a leucocytosis which may reach as high as 30,000 or 40,000. The recent experimental work of Wright and Livingstone serves to place these clinical observations on a sound basis. By injecting whole blood into the serous cavities of animals they found that they could produce a leucocytosis at will. If the blood failed to reach the peritoneal cavity the increase was very slight. The leucocytosis reaches its height in about ten hours, with a return to normal by the fourth day.

In *malignant disease,* both carcinoma and sarcoma, there is a moderate leucocytosis in about 60 per cent of cases. Epithelioma of the skin is not accompanied by an increase in the leucocytes, but high counts may be obtained in carcinoma of many of the internal organs, especially the alimentary canal. Post-digestion leucocytosis is very frequently absent in cancer of the stomach. The increased leucocyte count may fall to normal when the tumor is removed, only to rise again should it recur.

An *eosinophilia* may occur in such a variety of conditions that it is difficult to avoid giving a mere catalogue which is of little practical value. The more important conditions in which it may occur are;

(1) infections by animal parasites, particularly trichina spiralis, tenia saginata and hydatid cysts of the liver, ascaris lumbricoides, oxyuris vermicularis, and bilharzia; (2) skin diseases affecting a considerable area; (3) asthma; (4) diseases of the bone marrow such as myelogenous leukemia, sarcoma of the marrow, and osteomyelitis.

BLOOD TRANSFUSION

Blood transfusion has become so common a practice that some reference must be made in this place to the method of choosing a suitable donor. It is essential that the corpuscles of the donor should neither be hemolyzed nor agglutinated by the serum of the patient, nor the corpuscles of the patient by the serum of the donor. In point of practice it has been found that if the cells are not agglutinated, they will not be hemolyzed, so that it is only necessary to test for agglutination. Moreover the serum of the donor is so highly diluted when it enters the blood stream of the patient that it has no action on the patient's corpuscles. We only need to see, therefore, if the cells of the donor are agglutinated by the serum of the patient. This may be done in two ways:

1. By *matching* the cells of the donor against the serum of the patient, and observing whether agglutination occurs.

2. By *grouping* the blood of the donor and of the patient, and determining whether the groups will harmonize.

Matching.—Where blood transfusions are only done at long intervals, and no special serum is available, the blood of the donor may be matched against that of the patient. Corpuscles and serum are collected both from patient and donor. The corpuscles are obtained by collecting 2 drops of blood in 1 c.c. of a solution of 2 per cent sodium citrate in normal saline, the serum by collecting the blood in a Wright capsule and allowing the clot to separate. One drop of the serum is mixed with one drop of the cell emulsion on a cover glass and the mixture examined as a hanging drop. Agglutination will occur within 10 minutes if the bloods are incompatible, but it is wiser to wait for an hour. The macroscopic method may also be employed, the serum and cells being mixed on a slide, and the rapid appearance of a brick-red deposit indicating the occurrence of agglutination. In actual practice it is sufficient to test the donor's cells against the patient's serum.

Grouping.—The blood of all human beings may be divided into four groups, depending on the presence of isohemagglutinins. Some of these groups will not agglutinate others, some will. The approximate percentage of the different groups is as follows: Group I, 10 per cent, Group II, 40 per cent, Group III, 7 per cent, Group IV, 43 per cent.

The members of Group IV may be used as universal donors, for their corpuscles are not agglutinated by the sera of any other group. Members of Group I can receive blood from any other group, for their serum agglutinates the corpuscles of no other group. The remaining reactions are seen in the accompanying table.

Corpuscles (donor)	Sera (patient)			
	I	II	III	IV
I	0	+	+	+
II	0	0	+	+
III	0	+	0	+
IV	0	0	0	0

+ = Agglutination 0 = No agglutination

It will thus be seen that if we have known sera of Group II and Group III, we can determine to what group any donor or patient belongs. A drop of the known serum is mixed with a drop of the cell suspension, and agglutination looked for as before.

The great advantage of this method is that a list of donors belonging to known groups can be kept, and only the blood of the patient requires to be grouped.

Although a full discussion of the complex subject of blood groups would be out of place here, there are a few additional points which should be touched upon.

If the same donor is to be used after an interval of time for a second transfusion, even although the two bloods belong to suitable groups they should be matched again, otherwise alarming hemolysis and hemoglobinuria may occur, owing to the development in the patient's blood of agglutinins and hemolysins originally absent. Unless this precaution is taken a fatality may result.

It may not be safe for a patient in Group I (a universal recipient), who has previously received an injection of blood from a member of Group II, to receive another from a member of Group III, for the patient is no longer a pure Group I, but a combined Group I and II.

The work of Guthrie and Huck, published in 1923, indicates that there may be even greater complexity in the blood groups, and that there may be subgroups within the main group which may cause a slight reaction. The blood of persons shown to belong to the same group by the ordinary tests may therefore show isoagglutination when matched against each other. This is the probable explanation of the unexpected but slight reactions which occasionally occur even when the grouping is perfectly satisfactory.

In conclusion it may be well to mention that the grouping here given is that described by Moss in 1910. Janský arrived at similar conclusions in 1907, but unfortunately the members in the groups in the two classifications were transposed. As an attempt is being made to introduce the Janský classification, the result has been a regrettable confusion which may readily prove disastrous to the patient. When a donor states that he is in a certain group, it should always be ascertained which classification is being used.

References for Further Study

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Much useful applied bacteriology will be found in Choyce's System of Surgery, 2nd ed., 1923, and in the Nelson Loose-Leaf Medicine, 1920, vols. 1 and 2.

CHAPTER III

INFLAMMATION

Inflammation is the most important as it is the most universal of all pathological processes. Being the *local reaction of the living tissues to an irritant*, it follows that some degree of inflammatory change is present wherever the tissues are subjected to the action of an irritant. No matter, therefore, how aseptic an operation may be, it must inevitably be accompanied by some degree of inflammation.

This reaction of the tissues is a purposive one; its object is to free the body of the irritant. It is essentially a beneficent phenomenon. Its clinical manifestations are disagreeable to the patient, but they are to be understood and if possible guided rather than combatted.

Our comprehension of the inflammatory process is based upon the researches on phagocytosis with which the name of Metchnikoff will always be associated. It was Metchnikoff who showed that the introduction of an irritant into the body was the signal for certain of the wandering mesoblastic cells of the body to exert themselves to encompass its destruction and removal. At the time of his great discovery he was in no way interested in problems of immunity, being engaged on a zoological research into the intracellular digestion manifested by the mesodermal cells of the more lowly organized animals. It was not on the human body that these observations were made, but upon the transparent body of the star-fish larva. Metchnikoff introduced some rose thorns into this lowly organism, and next morning he had the delight of observing that they were thickly clustered about by the wandering cells whose function he had been trying to determine. In that hour Metchnikoff was transformed from a zoologist into a pathologist. The fundamental discovery had been made, and the passing years merely showed how fully this principle could be applied to the higher animals and to man. In the star-fish larva there is no vascular nor nervous system, so that we may say that the essence of inflammation is the reaction of the mesodermal cells against an external agent. The vascular and nervous changes are of secondary significance. As we ascend the animal scale the process becomes more complex, the development of a vascular system renders it more complicated, but even in man the object of all the intricate mechanism is the removal of the irritant by means of phagocytosis, although other humoral factors are introduced which will require to be duly considered.

The inflammatory process may be described as the formation of an inflammatory exudate, the function of whose cells is to devour and remove the irritant. In the higher animals certain striking vascular

phenomena are also present, but the object of these changes is merely to allow the wandering cells, which in these animals are for the most part contained within the vessels, to escape to the site of the irritant, which is nearly always extravascular.

Before proceeding to consider these two main phases of the inflammatory process we may pause to enumerate the principal causes of inflammation.

Causes.—The irritant which is the cause of inflammation may be either physical, chemical, or bacterial.

I. *Physical* irritants may be extremes of heat or cold (causing burn or frost bite), X-rays, radium, the presence of a foreign body, and most important of all, trauma. The knife of the surgeon in the most aseptic operation acts as an irritant, for not only does it act directly, but, by killing tissues in its passage, it calls forth an inflammatory reaction for their removal.

2. *Chemical* irritants when present in sufficient concentration may produce violent inflammation. Thus croton oil and strong acids or alkalis on the skin, arsenic and other metallic irritants in the bowel, and corrosive sublimate in its passage through the kidney act in this way.

3. *Bacteria* form by far the commonest cause of the inflammations met with in surgical practice. Some bacteria produce acute inflammation with a tendency to the formation of pus. These are classed as *pyogenic* or pus-forming organisms, of which the most important are the staphylococcus, the streptococcus, the pneumococcus, the gonococcus, the meningococcus, the Bacillus coli, the Bacillus typhosus, and the Bacillus pyocyaneus. Some bacteria produce a low-grade inflammation, more or less chronic in character, without the formation of pus, but with a well-marked defensive reaction on the part of the tissue cells. Such are the tubercle bacillus, the spirochæta pallida, actinomyces, and other slowly acting germs.

There are three main phases of the inflammatory process, each with its specific duty. These are the vascular changes, the formation of the inflammatory exudate, and the process of repair.

I. THE VASCULAR CHANGES

The feature of inflammation which attracts the attention of the clinician and the patient is the change which occurs in the blood vessels. It is not the essential feature, for the process of inflammation may occur in a non-vascular tissue such as the cornea, but it is the outward and visible sign of the inward change which is taking place, and it is largely responsible for the clinical signs characteristic of the condition.

When an irritant is applied to a part, when, for instance, the staphylococcus invades the finger or the colon bacillus the appendix, the vessels, mainly the small veins and capillaries, after a preliminary and brief contraction, dilate more and more, so that soon the part becomes red and congested, and the vessels are stuffed with blood.

The finger becomes red, hot, swollen, painful, and may throb owing to the increased volume of blood in the vessels.

The blood flow is at first quickened, but soon it becomes slower than normal owing to a number of factors such as increased viscosity of the blood from transudation of serum, and the obstruction of the endothelial cells which become swollen and project into the lumen. In mild cases the blood flow is maintained, but in more severe inflammation there may be actual stoppage or stasis, the vessel becoming

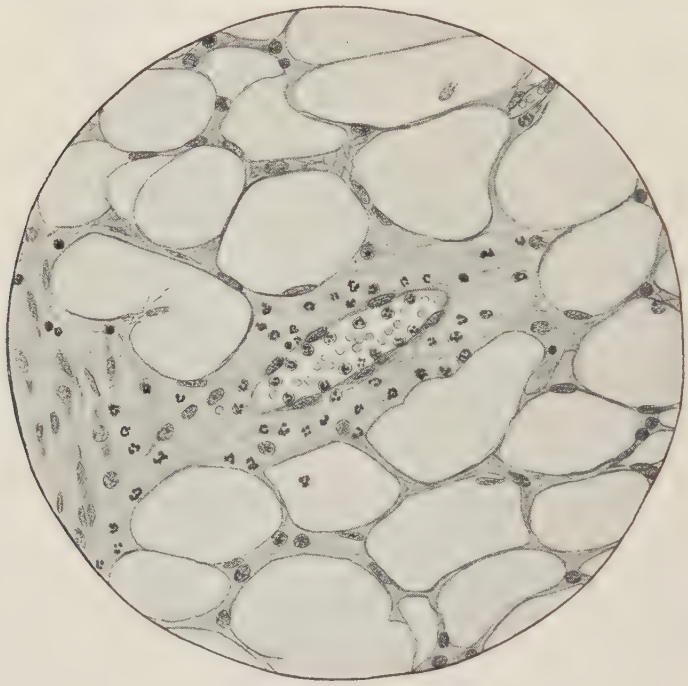

Fig. 1.—Acute inflammation in the omentum. Pavementing of the leucocytes along the wall of a capillary, together with free emigration into the surrounding tissue.

thrombosed. Complete recovery of the tissue may occur before but not after thrombosis has occured. With the slowing of the blood flow the formed elements of the blood undergo a redistribution, the leucocytes and platelets falling out into the peripheral stream, and approaching the sides of vessel until they form a regular pavement along it, whilst the red cells remain in the axial stream.

Meanwhile the cells of the vascular endothelium become swollen and much more prominent, project into the lumen of the vessel, and are less firmly cemented to their neighbors, so that potential spaces are formed between adjoining cells. Some of the cells proliferate and are cast off to take part in the formation of the inflammatory exudate.

The polymorphonuclear leucocytes forming the vascular pavement put forth protoplasmic processes or pseudopodia, which insinuate themselves through the spaces between the endothelial cells, and by means of ameboid movement soon pass completely through the vessel wall, to be followed later by less ameboid cells and red blood corpuscles. Outside the vessel the leucocytes collect around the irritant, drawn thither by the mysterious force we call chemiotaxis. It is as if they came in response to an S. O. S. call of distress on the part of the tissues. The whole process of the emigration of the leucocytes may be studied

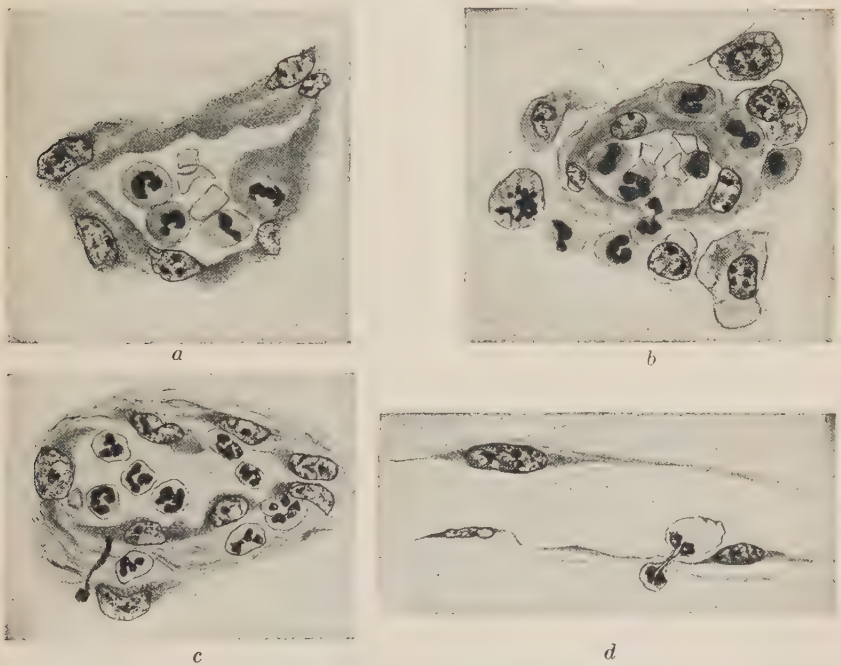

FIG. 2.—Acute inflammation. *a*, Mitosis of endothelial cell in wall of small vein; *b*, *c*, and *d*, emigration of polymorphonuclear leukocytes through the walls of small blood-vessels. (Mallory.)

under the microscope in the mesentery of the frog. In surgical material fixed immediately after removal the various stages may often be seen beautifully, for instance in the mesenteric attachment of an inflamed appendix. The migration of the leucocytes is accompanied by a serous exudation of plasma, which plays an important part in the action which follows, and is responsible for much of the swelling.

Such in brief are the vascular phenomena of inflammation. What is their purpose? They provide the mechanism by means of which the inflammatory exudate is produced. The formation of that exudate is the sole object of the inflammatory process, so that the vascular changes in themselves are meaningless.

II. THE INFLAMMATORY EXUDATE

The inflammatory exudate is formed (1) by the migrating cells from the blood, (2) by the blood plasma, (3) by certain cells of the tissues. The purpose of the exudate is to neutralize and overcome the irritant, to remove it, and to repair the damage done. Attempts at repair, indeed, may begin early in the process, and the various stages may all be seen in the same tissue.

1. The Blood Cells.—The *polymorphonuclear leucocyte* is the cell of acute inflammation. In acute pyogenic infections it may appear to be the only cell present. The number in the circulating blood is greatly increased, a condition of leucocytosis, owing to hyperactivity of the leucoblastic tissue in the bone marrow. The characteristic appearance of its lobed or multipartite nucleus and the fine neutrophil granules of its cytoplasm are too well known to demand description. In the early stages the outline is well preserved and the nucleus sharp and distinct, as in the red hepatization stage of a lobar pneumonia. Later the cells become degenerated, indistinct, and stain diffusely. They constitute the chief element of pus, but as pus cells they usually show marked granular degeneration. On disintegrating they liberate (1) antibacterial substances, (2) proteolytic ferments, and (3) thrombin which interacts with the fibrinogen in the plasma to form fibrin. They are actively ameboid and phagocytic, and their chief function is the destruction of living bacteria by phagocytosis.

The *lymphocyte* plays but a minor part in acute pyogenic inflammation, although it may be present in some numbers in the later stages. In chronic inflammation, and especially in the infectious granulomata such as tuberculosis and syphilis, it assumes a position of commanding importance, and the tissue which is the site of the lesion may be packed with these cells. It must be admitted, however, that many, if not most, of the "small round cells" seen in chronic inflammation may be derived from the tissues rather than from the blood. The lymphocyte appears to be an important, although frequently inadequate, means of defence against the spread of carcinoma, but here again the cells are probably histogenous rather than hematogenous in origin. The lymphocyte is little if at all phagocytic, and it appears to accomplish its work of defence by antitoxic rather than by phagocytic activity.

The large mononuclear, a cell larger than the lymphocyte, with indented or kidney-shaped nucleus and more abundant cytoplasm, can not be distinguished in the inflammatory exudate from the vascular and other endothelial cells presently to be discussed. Indeed it is not improbable that the large mononuclears are derived from these cells. Their function is to act as scavengers in the later stages of inflammation, removing by virtue of their great phagocytic power the dead bodies of leucocytes, bacteria, and tissue cells, and carrying them away in the lymph stream. They are therefore present in small numbers in the early, but become much more numerous in the later stages of inflammation. In typhoid fever they, together with the endo-

thelial cells, form the prominent feature, crowding the intestinal, glandular, and other lesions.

It may be noted here that infections characterized by a polymorphonuclear leucocytosis are not attended by a lasting immunity, whereas in those diseases such as typhoid fever and measles where the immunity is of long duration the defensive rôle is played by the lymphocytic and mononuclear series of cells. It has been suggested that the former are end products with no offspring, their home being the blood stream, whereas the latter are cells whose natural habitat is the tissues, although they may wander out into the blood, and they can pass on the immunity lesson to their descendants. Scarlet fever provides an exception to this general rule.

The eosinophil is a mysterious cell which appears in considerable numbers, but for no apparent object, in certain very diverse conditions. An eosinophilia in the blood is found in infection by animal parasites, in asthma, and in urticaria and other similar skin affections, all conditions in which an element of anaphylaxis plays some part. In asthma the bronchial mucous membrane may be crowded with eosinophils, and in many appendices the seat of chronic inflammation I have been struck with the extraordinary numbers of eosinophils particularly in the mucous and sub-mucous coats. As in the case of the lymphocyte, it is possible that many of these cells are derived from the tissues rather than from the blood.

Red blood corpuscles where present must be regarded as accidental. They have no function to perform, and have either passed through the openings made by the migrating leucocytes, or are due to rupture of the vessel caused by undue distension or by the toxic action of circulating poisons upon the vessel wall.

Phagocytosis.—The cells of the inflammatory exudate are collected about the irritant in order that they may have the opportunity of exercising their power of phagocytosis. The work of Metchnikoff has shown that phagocytosis is an almost universal endowment of cell life. It is by this power that the cells of the lower organisms absorb their nourishment; by means of it even the most resistant tissue, such as bone, is moulded into shape; it is the mechanism by which dead tissues are removed from the body; and finally it is the most efficient defense of the body against disease.

In the acute stage of inflammation the polymorphonuclear leucocyte is the most active phagocyte. It approaches the bacterium, pushes forth processes of protoplasm called pseudopodia or false feet, engulfs its prey, and digests it by means of the digestive ferment which it secretes. The absorbed body gradually disappears, and its former site is indicated by a digestive vacuole.

Other phagocytic cells playing an important part in inflammation are the large mononuclear leucocytes of the blood; the endothelial cells lining the blood vessels, the lymphatics, and the serous membranes; the wandering connective tissue cells; and the cells lining the bronchi and pulmonary alveoli. These cells, which may be grouped collectively

as the mononuclear cells of the inflammatory exudate, usually direct their attention to the absorption of dead cells and tissues, such as defunct leucocytes and red blood cells, blood pigment, particles of bone, etc., but they may also contain bacteria, especially those responsible for the more chronic types of inflammation, such as tuberculosis.

The task of removing these more chronic irritants sometimes leads to the formation of giant cells, which result from the fusion of a number of phagocytes to form one large cell containing numerous nuclei usually arranged around the periphery of the cell. These foreign body giant cells may be seen to great advantage when a foreign body such as a lycopodium spore is introduced into the tissues. They are present in tuberculosis, syphilis, actinomycosis, any form of bone destruction—in short in any condition where a somewhat refractory irritant has to be removed.

Although the bacteria engulfed by the phagocytes are usually digested, this is by no means always the case. Tubercle bacilli, meningococci, gonococci, may remain recognizable for long periods within the body of the phagocyte. Moreover they may actually remain alive, so that when the cell which contains them disintegrates they may be capable of producing further infection.

The degree of phagocytosis is usually an indication of the resisting power of the tissues. If phagocytosis is scanty or absent the prognosis is correspondingly grave. The phagocytic activity, however, is not entirely a function of the cell; it is dependant on antibodies in the exudate, opsonins, which bring the phagocyte into relation with the bacterium. On the other hand it is probable that many of the antibodies are produced by the inflammatory cells themselves. The exact degree of importance in the inflammatory process to be assigned to the cells on the one hand, to the body fluids on the other, is still a matter of debate.

The phagocytes which are unable to digest all that they have absorbed dispose of this material in several ways. Many carry it to the surface and discharge it on to an ulcer; many pass into the lymphatics and deposit it in the lymph glands; some retire into the blood stream and find a grave in the spleen, the liver, and other cemeteries of the body.

2. The Blood Plasma.—The plasma forms an important constituent of the inflammatory exudate. Normally passing as lymph from the capillaries into the tissues and being absorbed thence into the lymphatics, in inflammation it is poured out in such quantity that adequate absorption is impossible. It accordingly collects in the tissues, bringing with it antibodies such as agglutinins, bacteriolysins and opsonins. The amount varies greatly depending mainly on the site of the inflammation. It is specially abundant in lose subcutaneous tissue and in serous sacs, but even in such an organ as the appendix the muscle fibers may be widely separated by inflammatory edema. It is the chief cause of the swelling in inflammation, and in subcutaneous positions the edema may be recognized by the phenomenon of pitting on pressure.

The functions of the plasma are to dilute the toxins, to neutralize them, to injure bacteria by means of its antibodies, and to wash them away where that is possible, as on a free surface. The therapeutic possibilities of the plasma are recognized in Bier's method of hyperemic congestion, in which intense congestion and exudation of serum are produced by constriction of such a part as the finger, often with very beneficial results on the course of the inflammation.

Fibrin is formed as the result of the union of thrombin liberated from the shed leucocytes with fibrinogen in the plasma, and consists of an interlacing of fine threads. It is specially abundant on a serous surface such as the peritoneum or pleura, or on a mucous surface covered with stratified epithelium such as the pharynx. In the latter site it frequently binds together the necrosed epithelial cells to form a false membrane, which is firmly adherent to the surface. It is only present in small amount in deep inflammations, and is not found in an abscess where it has been digested by the proteolytic ferments of the leucocytes and bacteria.

In common with the other factors in the inflammatory process, fibrin has a useful purpose to perform. It is essentially protective and limiting. In appendicitis, for example, the fibrin endeavors to limit the process by attempting to shut off the inflamed area from the general peritoneal cavity. If the surface of the bowel is red, intensely congested, and shows no fibrin the prognosis is much worse than when it is covered with an abundant coating of fibrin. Be not therefore too eager to wipe away with the ever-ready swab a protective covering which may offend the eye of the surgeon rather than the tissues of the patient.

3. The Cells of the Tissues.—The cells of the inflammatory exudate are not derived from the blood alone. Many arise from the tissues. We may therefore distinguish two groups of cells, the one hematogenous, the other histogenous in origin.

These histogenous cells belong to the great group of the **wandering cells** of the body. Whilst most of the cells of the body are fixed in their position and anchored to one another, others are free and lead a wandering nomadic life until they perish. The wandering cells are concerned with the process of inflammation, the fixed cells with the process of repair. To the former class belong all the leucocytes of the blood, which are not only driven around in the blood stream, but possess the power of independent movement.

Many of the tissue cells are also free wanderers. They make their way through the interstices of the tissues by virtue of their ameboid movement, and when a living tissue is fixed instantaneously their long pseudopodia are often caught before they have time to retract. These are the cells which play an important rôle in the later stages of acute inflammation, and particularly in all forms of chronic inflammation.

Much difference of opinion exists as to the exact nature and origin of these different cells. Amongst a multitude of workers on the sub-

ject the names of Maximow, Marchand, and Mallory are specially worthy of mention.

There are three possible sources for the bewildering variety of wandering cells which hurry through the tissues to the scene of the

FIG. 3.—Group of polyblastic or wandering cells of various types: *ly.*, Lymphocytes; *pl.*, plasma cells; *ph.*, phagocytic cells of large size, some containing blood-pigment, others, *l.ph.*, containing much fat; *g.*, foreign-body giant-cell formed about granules and crystals of bismuth; *fibr.*, connective-tissue cell. (MacCallum.)

nearest inflammatory combat. (1). The endothelial cells lining the reticulum and lymph channels of the spleen, the lymph glands, and lymphoid tissue in the intestine. Mallory is the great champion of

the endothelial cell; he sees it everywhere. (2). The adventitial cells of Marchand, mononuclear cells which have at one time wandered out through the walls of the blood vessels and now lodge in their immediate vicinity. The familiar perivascular infiltration, so characteristically seen in syphilitic lesions, may be composed of these cells. They probably correspond with the clasmatocytes of Ranvier. (3). Lymphocytes of the blood which have migrated and become ameboid in the tissues. Maximow, in a series of very able papers on the etiology of inflammation, comes to the conclusion that most of the histogenous cells are of this origin, and therefore originally hematogenous in type. The lymphocytes after emigration develop into the large ameboid cells of irregular shape which Maximow names polyblasts, and amongst which he includes the plasma cell.

Of the cells of histogenous origin the most important are the lymphocyte, the plasma cell, and the endothelial cell.

The *lymphocyte*, often referred to in the tissues as the small round cell, has already been described as it occurs in the blood. Many of those present in an inflammatory exudate are formed from proliferation of the lymphoid cells of the perivascular lymphatic sheaths, a mode of origin which may be seen to best advantage in cerebral inflammation. In tuberculosis and syphilis it is the most important cell, and it has been shown that when the lymphoid tissue of the body is damaged by X-rays the resistance to tuberculosis is greatly lowered. In many chronic inflammations "round-celled infiltration" is a prominent feature. It may be found at the edge of tumors, especially epitheliomas.

The lymphocyte may replace the polymorphonuclear in the later stages of acute inflammation. This change can be watched in a case of acute meningitis, the cerebrospinal fluid of which is examined every day. Day by day as the patient improves the polymorphonuclears decrease and the lymphocytes increase, until only a lymphocytosis remains. The same may be seen in experimental infections of the peritoneum. These cells are derived from the connective tissues, not from the blood.

The *plasma cell* is found only in the tissues, never in the blood. It is probably derived from the lymphocyte. Characteristic in shape, when once seen it can readily be recognized. It is larger than a lymphocyte, irregular or polygonal in shape, with a round eccentric nucleus showing a clock face arrangement of granules, and an abundant basophilic cytoplasm in which there may be a clear area close to the nucleus. It is best demonstrated by means of Pappenheim's pyroninmethyl green stain; the nucleus stains green and the cytoplasm bright red. It is normally present in the intestinal mucosa, and may be present, sometimes in considerable numbers, in chronic inflammations, being seen to great advantage in the perivascular infiltration of the brain in general paresis, and in chronic inflammation of the cervix and the Fallopian tubes. Even in acute inflammations in the central nervous system the plasma cell and the lymphocyte may be the chief

cells present. Thus in encephalitis lethargica they are almost the only cells found, and in acute poliomyelitis they constitute the most important part of the cytological picture.

The *endothelial cell* of the tissues can not be distinguished by our present methods from the large mononuclear of the blood; indeed it is not improbable that the latter is derived from the former. The endothelial cells of the inflammatory exudate are formed by proliferation of the cells lining the blood vessels, the lymphatics, and the lymph spaces in the tissues. They perform the function already ascribed to the large mononuclears of the blood, namely that of scavengers. In the neighborhood of foreign bodies several may fuse together to form one large multinucleated giant-cell; such cells are best seen in tuberculosis.

III. REPAIR

Inflammation is in its essence a struggle between two forces representing destruction and conservation. In every case these two proc-

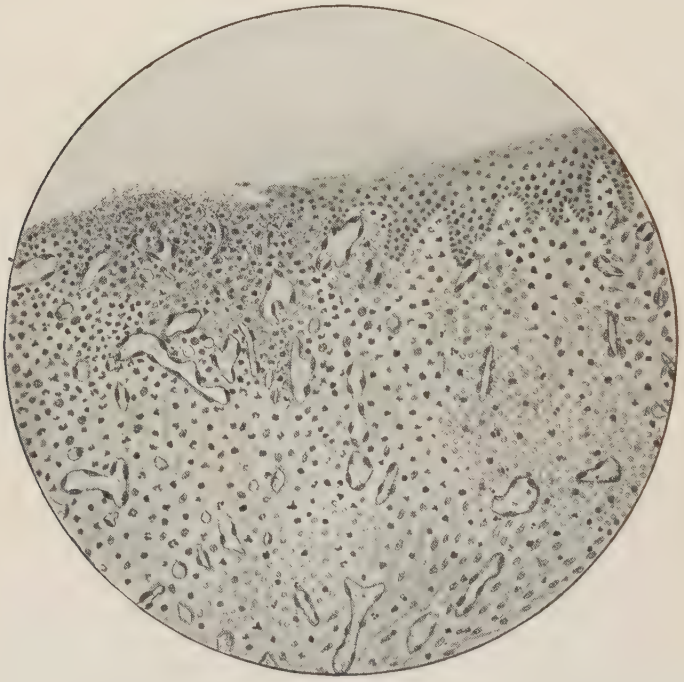

FIG. 4.—Inflammatory tissue. The surface epithelium is ulcerated, the underlying tissues are everywhere infiltrated with inflammatory cells, and granulation tissue has not yet begun to form.

esses are present. The end result depends on which proves the stronger, and upon the degree of destruction produced before repair sets in. To every case there are three possible terminations: (1)

resolution, (2) suppuration with tissue death, and (3) repair with fibrosis.

Repair is sometimes spoken of as a part of inflammation. This we cannot but feel is a mistake. It is true that the two processes are most intimately blended, and it is convenient to consider them both at the same time, but that does not mean that they are one and the same thing. MacCallum compares inflammation to a fire in which, while the flames are still burning fiercely in one part of the building and the fire engines are pouring on floods of water, gangs of carpenters have already begun to arrive, and are busy with reconstructive work on the burnt out portions. The two processes go on side by side, but they are quite independent of one another, and either zone may be absent. We have already seen that the cells concerned are also different; in inflammation it is the wandering cells, in repair the fixed cells of the tissues which are concerned.

The process of repair may conveniently be studied in two classes of cases: (1) healing of a wound with loss of substance, and (2) healing of an incised wound in which the edges are brought together without loss of substance. Although it is convenient to study the process in the case of a wound, it may be seen in any inflammation which goes on to recovery. Adhesions shutting off an inflamed appendix from the general peritoneal cavity, the zone of fibrous tissue which walls off a chronic cerebral abscess, the omentum overlying and adherent to a gastric ulcer which threatens to perforate, are examples of a general tendency to repair as much as the healing of a wound made by the surgeon's knife.

1. Healing of a Wound with Loss of Substance.—A clean aseptic wound with loss of substance is in the same condition as a healthy or healing ulcer, and the same changes occur in both. The gap in the surface is filled with various elements of the inflammatory exudate, chiefly coagulated plasma, bound together by interlacing strands of fibrin. The capillaries at the sides and base put forth solid buds of endothelium which grow into the mass, unite with one another, and become canalized and filled with blood, thus forming a network of **new capillaries.** In this way the exudate becomes vascularized, and the fibrin, which at first forms a scaffolding for this new formation, becomes absorbed before the new capillary loops.

At the same time the connective tissue cells proliferate, and develop into plump fusiform cells with vesicular nucleus and branching processes called *fibroblasts*, which support the capillaries and permeate the fibrin, forming an interlacing network throughout it. The fibrin appears to act as a stimulus to these new endothelial and connective tissue cells, possibly providing them with nourishment, so that the growth of this new tissue is most marked where fibrin is most abundant. The general direction of the capillaries is perpendicular, while that of the fibroblasts is parallel to the surface.

Owing to the prolific growth of this new vascular tissue the floor of the gap becomes covered with little, translucent, rosy, nodular

masses or granulations which rapidly fill in the gap, give the floor a velvety appearance, and bleed readily on account of their great vascularity. This new formation is called *granulation tissue.* It is best seen on a healing surface, and its presence indicates that healing is taking place. Such vascular connective tissue may be found in any organ, and beautiful examples are seen in inflammation of the appendix, Fallopian tubes, etc. Wherever it occurs it is called granulation tissue.

The fibroblasts lay down fine connective tissue fibers between the cells. These fibers increase in number and thickness until definite

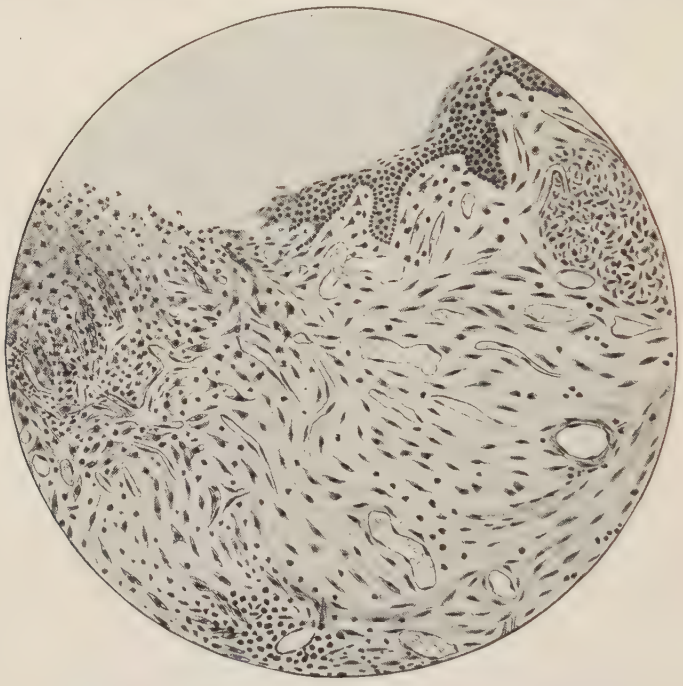

FIG. 5.—Granulation tissue and ulcer. The ulcerated surface is still composed of inflammatory exudate, but organization is proceeding in the deeper parts. The various stages of the process are well shown.

fibrous tissue can be recognized, and the originally cellular granulation tissue becomes gradually fibrosed. The fibroblasts are compressed between the bundles of new fibers, until they appear only as thin connective tissue cells consisting of little more than an elongated nucleus. The capillaries become obliterated, so that the vascular granulation tissue finally becomes a fibrous non-vascular mass of *scar tissue.*

Being non-vascular, scar tissue has less resisting power than normal tissue, so that it cannot endure the effect of trauma or bacterial infection so well as the surrounding healthy parts. Wherever scar tissue is found it shows a tendency to contract, and more damage may

PLATE I

Developing vascular tissue. Growth is proceeding from below upward (Maximow).

be done by this contraction than by the original inflammation. Thus a stricture of the urethra causing obstruction may be a more serious condition than the gonorrhea which produced it, and optic atrophy causes greater loss of vision than the optic neuritis which preceded it.

The *epithelium* at the edge of the wound or ulcer soon shows signs of proliferation, and a thin bluish-white line appears, which spreads inwards covering the surface with a layer of young epithelial cells. When scar tissue has formed the surface epithelium is white, bloodless, slightly wrinkled, and depressed below the surface from contraction of the scar.

A granulating surface presents a most efficient barrier against bacterial invasion. It is, however, easily injured, for the granulations are delicate, and the young epithelial cells struggling to gain a footing on the new surface are easily dislodged. The interfering and too vigorous swab, the over frequent change of dressings, the stream of strong antiseptic may do more harm than good. Free drainage should be provided for the escape of any discharge, and the granulating surface should be protected, but nothing should be done to interfere with that remarkable tendency to heal which is present in all healthy tissue.

2. Healing of a clean incised wound with no loss of tissue. Here there is no granulating surface, and yet the young vascular connective tissue which we have already recognized as granulation tissue forms the principal feature. Into the slit-like gap made by the knife blood plasma and whole blood are poured, which on clotting furnish the fibrin network that forms the scaffolding for the repair builders. Once more the capillary loops and young fibroblasts first use and then replace the scaffold, the capillaries absorbing any debris to be removed, and the fibroblasts "sewing together" the opposing surfaces.

The time required for complete repair will depend on a number of factors, of which the amount of tissue destruction and the degree of asepsis are the most important. The presence of bacteria will retard and may completely prevent the process. It is evident that it is impossible to give an estimate of the time required for a wound with loss of substance to heal, but the following table will give an indication of the approximate times of the various stages of the healing process in the case of an incised wound.

Healing of an Incised Wound

End of 12 hours:	Vascular and connective tissue reaction begins.
End of 2nd day:	Granulation tissue appears.
End of 4th day:	Temporary clot replaced by granulation tissue.
End of 5th day:	Epithelium covers narrow wound. Definite fibrils appear.
End of 3 weeks:	Dense non-vascular scar tissue is formed.

The process of repair with formation of granulation tissue and subsequent fibrosis may occur in any inflamed organ in which the process has passed the stage were resolution is possible, that is to say,

where there is tissue death and thrombosis of the vessels. The presence of fibrin in abundance appears to act as a stimulant to the formation of granulation tissue, possibly providing the cells of that tissue with nourishment. The formation of granulation tissue with fibrosis and consequent adhesions is therefore a prominent feature in inflammation of serous surfaces such as the pleura, pericardium and peritoneum. It is very remarkable and equally fortunate that in lobar pneumonia, where the amount of fibrin is enormous, no granulation tissue is formed except in rare cases of carnification of the lung. In an ordinary case resolution of the pneumonic exudate is complete.

THE COURSE AND VARIETIES OF INFLAMMATION

Although for descriptive purposes it is convenient to consider inflammation in a typical case, yet it must be borne in mind that there is no process which varies more in its course, its intensity, and its results. Of the main features of inflammation now one, now another may be emphasized, so that the picture may present the changing colors of the kaleidoscope, yet all are but variants of one process. The variations depend partly on the organ affected, but more on the relative strength of the attacking and defensive forces. We have already seen that there are three possible courses which may be followed, namely resolution, suppuration with tissue death, and repair with fibrosis. These will now be considered somewhat more in detail.

1. Resolution.—Up to a certain point inflammation may be completely recovered from, in which case resolution is said to have occurred. When bacteria invade the wall of the appendix the irritation calls forth the usual vascular changes and inflammatory exudate. If, however, the attack be weak or the defense vigorous, the bacteria are devoured and removed by the phagocytes, their toxins neutralized by the serum, any fibrin formed is dissolved, the inflammatory cells reenter the circulation, and the part returns to normal, bearing no trace of the conflict which has taken place, because there has been no actual destruction of tissue. In the same way a boil may resolve, without the formation of either pus or fibrous tissue. This, fortunately, is the usual course for inflammation to follow.

2. Suppuration with Tissue Death.—When the infection with virulent bacteria is intense, overwhelming the resistance, in addition to the formation of an abundant inflammatory exudate there is death of the tissue cells. Large numbers of these are killed by the bacterial toxins. Disturbance of the circulation due to thrombosis of the vessels may also play a part. At first the necrosed cells from a solid mass, but the proteolytic ferments of the numerous leucocytes soon produce liquefaction, so that the inflammatory area becomes a cavity or abscess, containing a fluid in which float living and dead leucocytes. This fluid is called pus. In such a case the part cannot return to normal, for the process of replacing the destroyed tissue will leave an indelible scar.

An abscess, then, is a cavity containing pus and surrounded by a wall of inflamed tissue. Taking as an example an abscess of the kidney, the kidney cells immediately lining the abscess cavity will be completely necrosed and disintegrated, those further out will show lesser degrees of degeneration such as cloudy swelling and fatty degeneration, and on the outskirts the cells will be healthy. Large numbers of bacteria are present in the wall.

In an abscess which has lasted for any length of time, whether or not it has been opened, a zone of granulation tissue is formed in the wall which separates the living from the dead tissue. It is remarkable

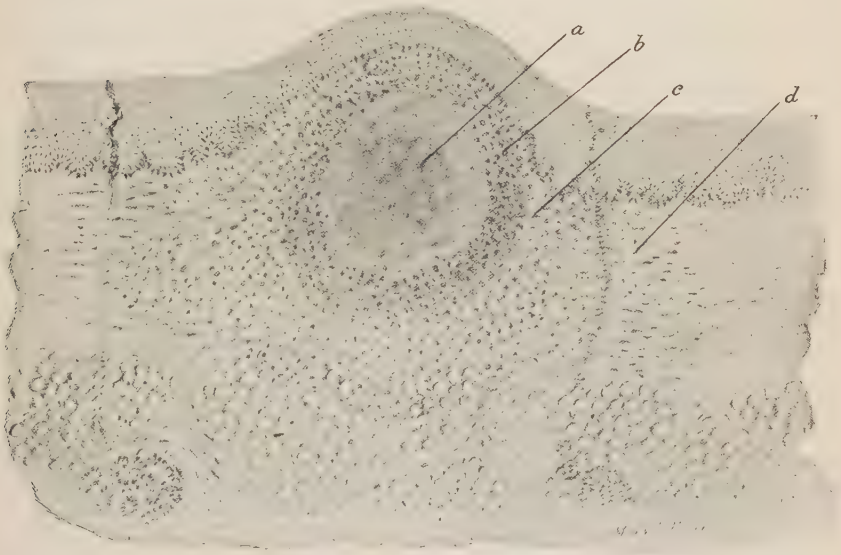

FIG. 6.—Formation of a furuncle. Showing, *a*, central core of pus; *b*, surrounding zone of densely crowded leukocytes; *c*, zone of less crowded leukocytes, and *d*, outer zone of fibroblasts. The epidermis is lifted and thinned by the pressure of the infiltration in the connective tissue below it (diagrammatic). (Keen's Surgery, Vol. I.)

for the numbers of large phagocytic endothelial cells which infiltrate its meshes. Owing to the fact that numerous pus cells or leucocytes are shed off from it, this lining is sometimes called the pyogenic membrane.

An abscess may advance, remain stationary, or recover. Should it advance, a progressive destruction of the cells occurs, so that more of the wall becomes liquefied and added to the central pus. Or it may burrow its way through the tissue, following the line of least resistance, and opening on the surface. To become stationary is uncommon, but a chronic liver abscess or a pyosalpinx may become walled off by fibrous tissue, and neither advance nor recover. Finally, when the abscess has discharged on a surface or has been opened by a surgeon

recovery will commence, the cavity being quickly filled by granulations springing from the surrounding walls. Even without discharging on a surface a small abscess may become invaded by granulation tissue and ultimately fibrosed, but this is not of common occurrence.

A boil is an example of an abscess located in a hair follicle or a sebaceous gland, the infection having penetrated the skin through the opening of one of the ducts as the result of friction or pressure. The usual invader is the staphylococcus aureus. Should the infection penetrate to the deeper layers of the skin and the subcutaneous fat, a *carbuncle* may be formed; this consists of a series of communicating

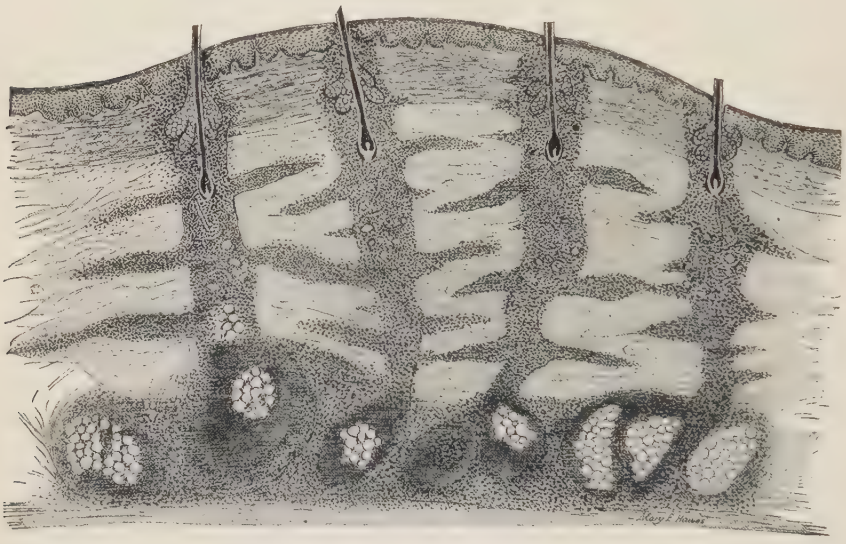

Fig. 7.—Section of a carbuncle of the back, showing infiltration of the adipose layer of the cutis vera and extension toward the surface through the columnæ adiposæ. (Keen's Surgery, Vol. I.)

abscesses which discharge by separate openings on the surface. In both of these cases there is a marked fibroblastic reaction which imparts a characteristic induration to the lesion.

An ulcer is an abscess which discharges on the surface. The histological structure is the same. There is the same purulent discharge, the granulating wall, the surrounding area of damaged cells. The pus is free to escape so that repair can take place by the growth of granulations filling the cavity, provided that the infection be overcome so that a "healthy ulcer" is produced.

A healthy ulcer or healing sore presents a floor covered with firm, pinkish-red, translucent granulations, covered with a slight serous exudation in which are a few pus cells. The edge is sloping and is bordered by a thin, bluish-white layer of young ingrowing epithelium.

The surrounding parts are normal, apart from a slight degree of hyperemia.

An ulcer may remain *unhealthy* owing to unfavorable local or general conditions, of which bacterial infection and defective circulation are the most important.

When the virulent bacteria are still present there is no attempt at repair, the base of the ulcer has an angry appearance and is bathed with thin yellow pus, the edges are ragged and irregular due to tissue destruction still going on, the discharge is profuse and offensive, and the surrounding parts are hot, red and edematous.

When defective circulation is the important factor, as in the ulcer on the lower third of the leg often associated with varicose veins, the base is covered with soft edematous, unhealthy-looking granulations (popularly known as "proud flesh"), the edges become sclerosed from formation of fibrous tissue, and the epithelium shows no sign of ingrowth.

The tuberculous ulcer is seen typically in the neck in cases of discharging tuberculous glands. The base is pale and ragged, and often

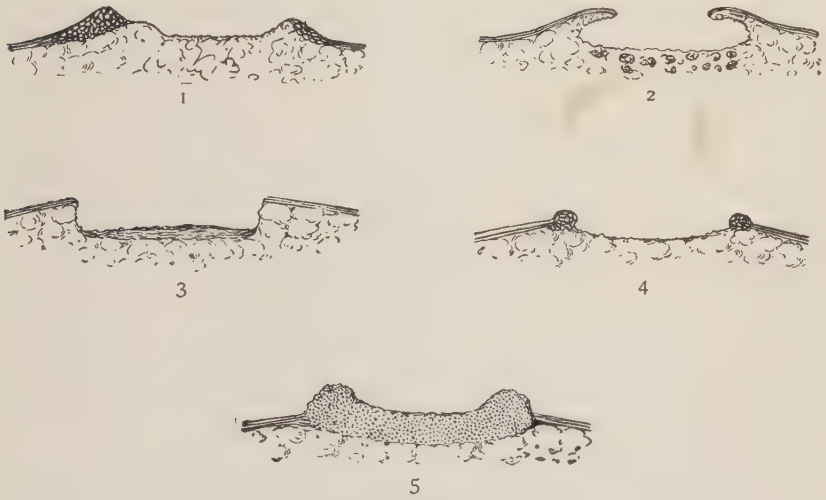

Fig. 8.—Varieties of ulcers: 1, Simple healing ulcer; 2, tuberculous ulcer; 3, syphilitic ulcer; 4, rodent ulcer; 5, epitheliomatous ulcer. (After Rutherford Morison.)

covered with gray sloughs, the edges are bluish in color, thinned out and undermined so that a probe may be passed for some distance underneath them. The discharge is thin and watery, and contains shreds of necrosed tissue.

The *syphilitic ulcer* presents a characteristic sharp, punched-out appearance, with a base like dirty wash-leather, and an outline that is often serpiginous. The edges are raised and indurated, and the discharge thick, glairy, and offensive. A common situation for such ulcers is the upper third of the leg.

A sinus is a tubular ulcer, which refuses to heal, owing usually to the presence of dead tissue. It is lined by granulation tissue. Many persistent sinuses prove to be tuberculous.

A *fistula* is a similar passage connecting a skin with a mucous surface, caused by an abscess discharging by separate openings on these two surfaces.

Pus is a yellow material with an alkaline reaction, consisting of leucocytes living and dead, mainly polymorphonuclears, although lymphocytes and endothelial cells may also be present and occasionally necrosed tissue cells. It usually contains living bacteria, but in such a condition as a pyosalpinx of long standing or a chronic abscess of the brain or of bone it may be sterile owing to the infecting bacteria having died out. Its physical characters differ somewhat with the infecting organism and the site of the infection. Pus cells in a gonorrheal discharge are well preserved, those in an empyema are much disintegrated, the difference being due to the difference in age of the exudate. The pus in staphylococcal infection is creamy in consistence and has a mawkish odor, that in streptococcal infection is sero-fibrinous in consistence and without odor. Tuberculous pus is flaky, that due to B. pyocyaneus has a greenish or blue color from the pigment pyocyanin, that of a brain abscess has also often got a green tinge, perhaps for the same reason, whilst the pus of B. coli infection has a characteristic fecal odor.

Septicemia and Pyemia.—The products of bacterial action may be absorbed into the blood, giving rise to sapremia, or the bacteria themselves may enter the stream, a condition of septicemia.

Sapremia is a condition of intoxication due to the action of saprophytic bacteria. These are unable to invade the living tissue, but flourish in dead tissue such as occurs in a wound with extensive laceration of the soft parts or in the remains of a placenta retained in the uterus. Owing to the great proteolytic power of the saprophytes the proteins are decomposed into toxic products, which when absorbed produce symptoms of intoxication. When the toxin factory is destroyed, as by scraping out the uterus or "débridement" of a wound, the symptoms rapidly subside.

Septicemia in itself is not necessarily a serious condition, for bacteria circulate in the blood stream in every case of pneumonia and typhoid fever. When, however, secondary foci of inflammation are set up in distant parts, the condition is called *pyemia*, and is one of great gravity. The secondary foci are not due merely to the settling down of circulating bacteria, but to the lodgement of septic emboli formed by the breaking-up of an infected thrombus or a vegetation from an inflamed heart valve.

The common sites for the formation of a septic thrombus are the middle ear, with infection of the lateral sinus and the formation of abscesses in the lung and later in the viscera generally, the appendix, with secondary abscesses in the liver, the uterine veins in puerperal sepsis, and the hemorrhoidal veins. After the formation of pyemic foci

in the organs has been established, the joints are liable to become infected, the inflammation varying from a mild arthritis to complete destruction of the joint.

The clinical signs of septic thrombosis with pyemia are very characteristic, namely, a series of severe rigors accompanied by marked fever occurring about every 24 hours, the patient feeling comparatively well in the interval. When the primary focus of infection is removed or cut off from the general circulation it is remarkable how quickly recovery may set in, even although secondary abscesses have been formed. The best example is the effect of tying the internal jugular vein in septic thrombosis of the lateral sinus.

FIG. 9.—Portal pyemia; abscesses of the liver secondary to suppuration in the appendix. (After Rutherford Morison.)

The post-mortem appearances in septicemia and pyemia are characteristic. In septicemia there may be marked decomposition, and rigor mortis is but little marked. Petechial hemorrhages are present in the pleura, pericardium, and endocardium. The blood is fluid and dark. The spleen is enlarged, soft and friable. The muscles and the heart are friable and stained red. The lining of the blood vessels is similarly stained owing to decomposition of the red blood cells. In pyemia, in addition to the above findings, small embolic abscesses may be present in the lungs, heart, kidney, liver, and other organs. These abscesses lie mostly just under the surface of the organ. The pleural and pericardial cavities may contain pus due to spread of infection from these abscesses.

3. Repair with Fibrosis.—The process of repair has already been studied. Its most important clinical feature is the formation of fibrous tissue with consequent thickening and contraction. The mechanical effects depend upon the site.

In the skin there will be a scar, always a point of weakness. In serous membranes such as the pleura and peritoneum there will be adhesions, which may or may not cause subsequent trouble. A personal factor has to be reckoned with in certain cases, for in some patients adhesions appear to form with much less provocation than in others. A tube will be stenosed, the nature of the functional disturbance depending upon the organ involved. Thus in the urethra or ureter there may be hydronephrosis, in the Fallopian tube or epididymis sterility, in the bile duct distension of the gall bladder, in the appendix repeated attacks of inflammation from narrowing of the outlet, in the esophagus difficulty in swallowing. Cysts may be formed, in the breast from obstruction to the lactiferous ducts, in the ovary from sclerosis preventing dehiscence of the follicles. In the heart the effect of fibrosis will be interference with muscular contraction, in the retina blindness, in the ear deafness, in the thyroid myxedema, in the peritoneum adhesions, in the pancreas interstitial pancreatitis with possibly a subsequent diabetes.

The three main courses of inflammation have been considered, but the varieties are endless, depending partly on the nature and virulence of the irritant, partly on the tissue involved.

A *purulent* inflammation is one in which suppuration with formation of pus is the prominent feature.

Should fibrin formation be marked, as in inflammation of serous membranes such as the pleura and peritoneum, the inflammation is called *fibrinous*.

The term *catarrh* is applied to a mild inflammation of a mucous membrane in which the irritant acts as a stimulant to the mucous cells. These pour out an abundant secretion of mucus which mingles with the serum of the inflammatory exudate to form a thin watery or sticky discharge containing a varying number of leucocytes and desquamated epithelial cells. Examples of catarrh may be found in any mucous membrane, for instance cold in the head, bronchitis, gastritis, mucous colitis, catarrhal appendicitis. When the injury is greater there is death of the cells, and a more abundant inflammatory exudate, so that the condition becomes purulent.

Finally in very severe inflammation of a mucous membrane there may be great necrosis of cells, and when these are bound together by fibrin into a membrane adherent to the surface the inflammation is called *membranous* or *diphtheritic*. The best example is provided by diphtheria, but other severe irritants such for instance as steam, may produce a similar condition in the throat.

It is possible to multiply almost ad infinitum the different varieties of inflammation, giving each a name, but to do so is merely to cloud counsel, for in every case the basic changes are the same, resolution,

suppuration, or repair with fibrosis, as the theme, in Adami's happy phrase, runs in a piece of music all but hidden under variations.

CHRONIC INFLAMMATION

Inflammation is usually divided into acute and chronic forms. For clinical purposes this is convenient, but from the pathological point of view these are but two phases of the same process. Acute inflammation is due to the action of an acute irritant, is marked clinically by heat, redness and swelling, and pathologically by hyperemia and exudation. Chronic inflammation is due to the action of a chronic irritant, there is no heat or redness, although swelling may be present, and the pathological feature is the abundant formation of new tissue. The polymorphonuclear is the cell characteristic of acute inflammation, for the reason that in the acute condition phagocytosis seems to be an important factor in defence. The lymphocyte, endothelial cell, and plasma cell from the bulk of the inflammatory cells in the chronic form, although the exact part which they play is as yet uncertain.

Chronic inflammation may be the *sequel to an acute attack* or may be chronic from the beginning. After an acute attack the irritant may not be completely removed and may remain to produce a chronic inflammation. After an attack of pharyngitis or cystitis a certain balance may be established between the attacking and defending forces, as a result of which bacteria linger in the pharynx or bladder giving rise to chronic inflammation. An acute osteomyelitis may leave behind a sequestrum which produces such a degree of chronic inflammation that the bone becomes greatly thickened. As long as pus remains in the pleural cavity the inflammatory process will continue. In these instances an irritant is still at work. We must not confuse with this condition the much commoner one of fibrosis and thickening due to a previous acute inflammation. The appendix thickened from previous acute attacks is not an example of chronic appendicitis. In the heart fibrosed as a result of an acute myocarditis there is no real chronic myocarditis. A thickened pleura is not necessarily the site of a chronic pleurisy.

The inflammation may be *chronic from the beginning.* A non-bacterial irritant such as a foreign body may act in this way. Pyogenic bacteria do not act thus, but certain slow-acting bacteria, of which tuberculosis, syphilis, actinomycosis and leprosy are the most important, produce a slow inflammatory reaction marked by proliferation of the endothelial cells, lymphocytes, and in some cases the plasma cells, with the formation of an abundant granulation tissue, at first cellular, but later becoming fibrosed. For this reason these conditions are grouped together as the infectious granulomata.

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CHAPTER IV

GANGRENE

Gangrene is death of a part en masse, and the dead portion or slough is large enough to be seen by the naked eye. In ulceration, on the other hand, the death is "molecular," and the dead particles are too small to be seen by the naked eye.

The death of a part may naturally be brought about in a great variety of ways, so that it is difficult to give a clear and simple classification of the causes and clinical varieties of gangrene. Speaking very generally, however, it may be said that gangrene is due either (1) to interference with the circulation of the part, or (2) to the action on the tissues of bacterial toxins. In ordinary civil practice by far the more important is the first of these groups. Frequently the two are combined.

A very useful clinical classification is into *dry* and *moist gangrene*. Dry gangrene is caused by a sudden arrest of the arterial blood supply to a part, especially to a portion of a limb. The blood drains out of the tissues, which become dry and shrivelled. Moist gangrene is due to the second great cause of gangrene, namely, the action of bacterial poisons on the tissues.

DRY GANGRENE

The most characteristic example of dry gangrene is that known as senile gangrene, in which the gangrene is a slow and gradual process the result of occlusion of the artery to the part by atheroma with a superadded thrombosis. It is most commonly seen in the foot, and usually begins in the big toe. In other cases the obstruction is more sudden, owing to the impaction of an embolus or the ligation of one of the main arteries to the part. In health the collateral circulation is usually quite adequate to supply the call for additional blood, so that gangrene does not develop. If, however, there is widespread vascular disease, if the heart is weak, if the resistance of the tissues is lowered by the long illness of the patient, the call for help, although indeed heard, can not be responded to, and the part will die. In deciding, therefore, upon the ligation of a main artery these considerations must be borne in mind.

The tissues being drained of their blood, the part becomes dried up and mummified. The skin is wrinkled, and at first is greasy and more or less transparent owing to the liberation of fat from the tissues, but soon the hemolysis of the red blood corpuscles leads to a discoloration at first greenish and finally black from the sulphide of iron which is formed. The term mummification is a singularly appropriate one,

PLATE II

Dry gangrene (Coley).

for the dry and shrivelled foot is exactly like that of a mummy, and when removed may be preserved dry and intact for an indefinite period. The dryness, however, is most marked at the surface where evaporation is free, and in many cases the interior may retain a considerable amount of moisture. Neuralgic pains are frequent and troublesome; they may be due to an accompanying neuritis.

The tissue cells undergo the ordinary changes characteristic of *necrosis*. The cytoplasm loses its normal granular appearance, and becomes hyaline or vacuolated. The muscle fibres lose their transverse striations. The nuclei become broken up into fragments (karyorrhexis), or dissolve and lose their staining properties (chromatolysis). The red blood cells are hemolyzed, with liberation of the hemoglobin.

A very definite bright red *line of separation* soon appears between the living and the dead tissue. This line indicates a process of inflammation due to the contact of the dead with the still living tissue. There is a dilatation of vessels and an exudation of leucocytes, and into the inflammatory exudate granulations begin to sprout from the living tissue. These granulations soon erode the dead tissue at the line of junction, and in course of time complete separation may occur. As the blood supply of the skin and subcutaneous tissues is less abundant than that of the muscles and bone, the destruction of the former will proceed further up the limb than that of the latter, so that the resulting stump will be conical in form.

Dry gangrene may be due (1) to gradual vascular obstruction as is seen in senile gangrene, and the allied conditions of diabetic gangrene, thromboangiitis obliterans, and Raynaud's disease; (2) to more sudden vascular occlusion as in embolism, thrombosis, ligation, or injury of the vessels; (3) to extreme cold; or (4) to the action of escharotics.

Senile Gangrene.—The arteries, particularly those of the leg, are frequently so occluded in old people as the result of atheroma or of medial sclerosis complicated by atheroma (see Chapter XXVIII) that a mere trickle of blood reaches the part. No pulse can be felt at the ankle in the rigid and tortuous vessels, and the foot is cold and numb. The calcified vessels form a striking feature in an X-ray picture. The tissues are just alive and nothing more, so that an injury of a trifling nature, such, for instance, as may be received while cutting a toe-nail, may give rise to a slight inflammation which is yet sufficient to produce extensive stasis in the sluggish blood stream, and results in the development of gangrene. Thrombosis of the narrowed vessel may complete the occlusion, in which case the gangrene will develop spontaneously.

The gangrene usually commences in the big toe as a dark-blue patch, or an indolent sore may appear, which in such circumstances should always be regarded with grave suspicion. The condition advances slowly but steadily, for the presence of the dead tissue gives rise to inflammation, which in turn is followed by stasis and gangrene, until a level is reached at which the inflammatory reaction is sufficiently active to lead to ulceration. The rate at which the line of

demarcation forms affords a hint as to the prognosis. Rapid formation indicates a more satisfactory condition of the circulation than a slow and long drawn out process.

It not infrequently happens that after the line of demarcation has formed the upward spread of the gangrene recommences, owing to the low vitality of the tissue being unable to cope with the inflammation at the junction between the dead and living tissue. It is obvious that under such circumstances operative interference is not to be lightly undertaken, for flap after flap may become the seat of gangrene at ever higher levels.

Fig. 10.—Atheromatous arteries in a man of sixty-one shown by the *x*-rays. (Keen's Surgery, Vol. V.)

Diabetic Gangrene.—Diabetic gangrene may be regarded as a form of senile gangrene in which the process is modified by the presence of sugar in the tissues which offers an ideal pabulum for bacterial growth. It is confined to elderly persons, and is essentially due to arteriosclerotic changes in the vessels either occurring coincidentally or arising as the result of the sugar in the blood.

Its onset is exactly like that of senile gangrene, so that in every case of apparent senile gangrene the urine should be tested for sugar.

It begins as the result of a slight injury, and usually appears on the big toe or on the sole of the foot where a perforating ulcer may be formed. At first the process is a dry one, but the parts soon become moist, swollen, edematous, and of a dusky red color, owing to the entrance of bacteria. The upward extension is much more rapid than in senile gangrene, and there is little tendency to self-limitation by the formation of a line of demarcation.

It must be remembered that in senile gangrene sugar may make a temporary appearance in the urine, only to disappear when the gangrenous part is removed.

Gangrene Due to Thrombo-angiitis Obliterans.—A form of gangrene which is closely allied to senile gangrene may occur in young men, usually Russian Jews, between the ages of 20 and 40. The vascular lesion, a combination of endarteritis obliterans and thrombosis, but affecting the veins as well as the arteries, is fully described in Chapter XXVIII. The vessels of the feet are the chief sufferers. The patient suddenly feels pain, burning, and tingling in the feet, which become pale and cold, and no pulse can be felt at the ankle. Gangrene of the toes may develop, which pursues the same course as senile gangrene.

Gangrene Due to Raynaud's Disease.—In Raynaud's disease a condition of "symmetrical gangrene" may develop, affecting the fingers more often than the toes. It is due to spasm of the arterioles, the basis of which is supposed to be a neurosis. Attacks of local syncope, in which the part becomes pale and cold, are followed by attacks of local asphyxia, in which the great dilatation of the vessels leads to an extremely sluggish circulation, so much so indeed that stasis and finally dry gangrene may develop.

Gangrene Due to Sudden Vascular Occlusion.—The occlusion may be due to embolism, to thrombosis, or to the ligation of a large artery.

Embolism.—When the vascular system is in a state of health the sudden occlusion of a vessel by an embolus is unattended by any untoward consequences, except in the case of the end arteries to certain of the viscera, when infarction may result. Even when the main artery of a limb is tied, the collateral circulation is sufficient to maintain the nutrition of the parts. When, on the other hand, the vessels are the seat of widespread arteriosclerosis, such a sudden occlusion is frequently followed by gangrene.

The first evidence of obstruction is intense pain at the point of impaction of the embolus. Pulsation in the vessel is normal above the obstruction but absent below it. The part affected becomes quite white at first, although the collateral circulation may restore the color to some portions of it. Dry gangrene soon develops, dry, because the venous outflow is unimpeded. If, however, the embolus is a septic one, as is usually the case when it originates in an acutely inflamed heart valve, or if bacteria gain entrance from without, the gangrene will develop into the moist variety.

Arterial thrombosis is usually due to disease of the wall of the artery, the narrowing of the lumen and the roughening of the surface being the important factors. Occasionally, however, it may be due solely to certain infective and exhausting diseases, of which the principal is typhoid fever. Venous thrombosis is even more common in typhoid, and there are cases in which this has been the only lesion accompanying gangrene, but in such cases the general debility and toxemia are important factors, for venous obstruction in itself is not sufficient to lead to gangrene.

Trauma may so injure the vessels of a limb that gangrene results at some distance from the site of injury, a condition known as indirect traumatic gangrene. The vessels may be ruptured by a direct injury, such as the passage over the limb of a cart wheel, or they may be torn by a fragment of broken bone. If the artery alone is damaged the gangrene will be dry; if the vein also is injured the gangrene will be moist.

Gangrene Due to Cold.—Intense cold produces frost-bite in two ways: (1) by causing such extreme contraction of the small arteries that the tissues die as the result of the anemia; (2) by the direct action of the cold on the tissues, a factor of minor importance. The vascular changes, however, may not only be disastrous because of the extreme constriction, but may be equally disastrous because of the extreme dilatation which follows unduly rapid thawing-out of the part. If the frozen part be exposed to undue heat the vessels dilate to such an extent that stasis and thrombosis occur, so that a limb which could have been saved owing to death of the tissues not having actually occurred may be sacrificed as the result of injudicious treatment. The gangrene is of the dry variety, and follows the same course as in the senile cases.

Gangrene Due to Escharotics.—A strong acid or a strong alkali applied locally will produce necrosis. The former gives rise to dry gangrene, for the acid coagulates the fluids of the part; the latter gives rise to moist gangrene, for the alkali causes liquefaction of the tissues.

Carbolic acid, even in so weak a dilution as 1 in 100, may produce gangrene of a finger when applied in the form of a soak. A 1 per cent solution will produce gangrene in 24 hours, a 2 per cent in 12 hours, and stronger solutions in even shorter time. The gangrene is due in part to thrombosis of the vessels, in part to direct action of the poison on the tissues.

MOIST GANGRENE

The essential difference between moist and dry gangrene is that in the former the venous blood is retained in the part, as a result of which saprophytic bacteria are enabled to flourish abundantly upon the dead tissue, and produce putrefactive changes.

The disease is seen in characteristic form as the result of injury to the main artery and vein of a limb; no fresh blood can enter so that

the tissues die, and no blood can leave the part, so that liquefaction and bacterial infection occur. The limb is cold, pulseless, swollen, and edematous. The color varies between dark-red, green, purple, and black, owing to the sulphuretted hydrogen produced by the putrefactive bacteria acting upon the liberated hemoglobin with the production of sulphide of iron. The skin, which is moist and macerated, becomes raised into blebs which contain foul-smelling fluid or gas. The horrible odor is due partly to nitrogenous products such as indol and skatol, partly to non-nitrogenous products such as sulphuretted hydrogen, butyric acid, and lactic acid.

The disease spreads rapidly up the limb, and there is little attempt at any formation of a line of demarcation. Indeed before such a line can be formed the patient is usually dead as the result of septic absorption. The constitutional symptoms are always grave, in marked distinction to the condition of the patient in dry gangrene.

In addition to gangrene resulting from injury to the main vessels of a limb the following are the principal varieties of moist gangrene: gangrene from acute inflammation, bed sores, gas gangrene, phagedena, and cancrum oris.

Gangrene from Acute Inflammation.—When an inflammatory exudate is rapidly formed in a dense and unyielding tissue, gangrene may ensue owing to the pressure of the exudate upon the vessels and the consequent cutting off of the blood supply. As the result of injury the deeper tissues may be badly torn whilst the skin escapes comparatively easily. Should infection supervene the pressure of the exudate on the vessels may cause extensive gangrene.

The best examples of inflammatory gangrene, however, are provided by boils, carbuncles, and necrosis of bone. The effect is particularly noticeable in bone, where the vessels are confined within such rigid canals that a mild degree of inflammatory swelling may result in the death of a portion of bone, especially if the periosteum be stripped off the bone by the formation of pus. The core of a boil and the slough of a carbuncle are examples of gangrene due to the same cause, and are to be distinguished from the molecular necrosis seen in an abscess of looser tissues.

Bed-sores.—A bed-sore is an example of pressure gangrene, developing over the sacrum, buttocks, and heels. Pressure alone, however, will not produce a bed-sore, for a healthy person may lie in bed for a year without developing one. The additional factors are a devitalized condition of the tissues as the result of old age or long illness, hypostasis from feeble circulation, and occasionally disease or injury of the spinal cord, which gives rise to an acute bed-sore. The only difference between an acute and a chronic bed-sore is the remarkable rapidity with which the former develops and spreads, and the fact that occasionally it does not develop at one of the usual points of pressure. It is not due, as used to be thought, to disturbance of hypothetical trophic centres in the spinal cord, but is more probably due to capillary stasis from injury to the vasomotor nerves.

The essential cause of a bed-sore is thrombosis due to continued pressure. A dusky reddish patch appears at the point of pressure, and the color deepens till it may be almost black. Blisters may rise and burst, and a greyish black slough forms which gradually separates, leaving a large granulating surface. The sore may be of any depth, and not infrequently exposes the underlying bone. Bacterial infection is invariable, and the resulting septic absorption is a most serious feature of the condition.

Gas Gangrene.—Gas gangrene, a condition formerly known as acute traumatic emphysematous gangrene, although fortunately comparatively rare in civil practice, was so appallingly prevalent during the war that great advances have been made in our knowledge of the disease.

The *bacteria* causing the condition are three in number, all of them anerobic bacilli: (1) Bacillus welchii or B. aërogenes capsulatus; (2) Vibrion septique, probably identical with the bacillus of malignant edema; and (3) Bacillus edematiens. To these may be added a fourth, Bacillus sporogenes, which, although neither causal nor gas-producing, is responsible for much of the horrible odor so characteristic of the disease.

These bacteria are putrefactive. They have the power of breaking down dead tissue, and their toxins and the gases they produce may seriously impair the vitality of living tissue, but they are unable of themselves to gain a footing in healthy tissues. In the war wounds the preliminary injury was due either to the direct trauma produced by a projectile, or to the cutting off of the blood supply to the part. The anerobic bacteria introduced into the wound on pieces of clothing, etc., then got, and seized, their opportunity.

The disease is essentially an affection of muscles, and the connective tissue may be, at first at any rate, comparatively little affected. Moreover the spread is longitudinal rather than transverse. The infection readily spreads from end to end of a muscle, but may be unable to spread from one muscle to another.

The affected muscle is at first dull and opaque, brick red in color, and resembles cooked meat. Even at this stage it is dead, for it does not contract when pinched nor bleed when incised. Bubbles of gas which can be pressed up and down between the fibres may be evident to the naked eye. Soon it softens and becomes diffluent, the color changing to green, brown, or black. The exudate is blood-stained. Gas can be felt in the tissues over an area considerably greater in extent than that of the dead tissue. The odor of the gas is extremely foul.

The *microscopic appearance* of the growing edge, as described by McNee and Dunn, throws a flood of light upon the spread of the disease. The first change observed is a separation of the muscle fibre from the surrounding interstitial tissue by a clear space, which McNee and Dunn consider to be filled with a toxic fluid. The fibre itself loses its striations, and stains a uniform eosin tint. At a later stage the sarcolemma disappears, and finally the entire muscle fiber disintegrates. The

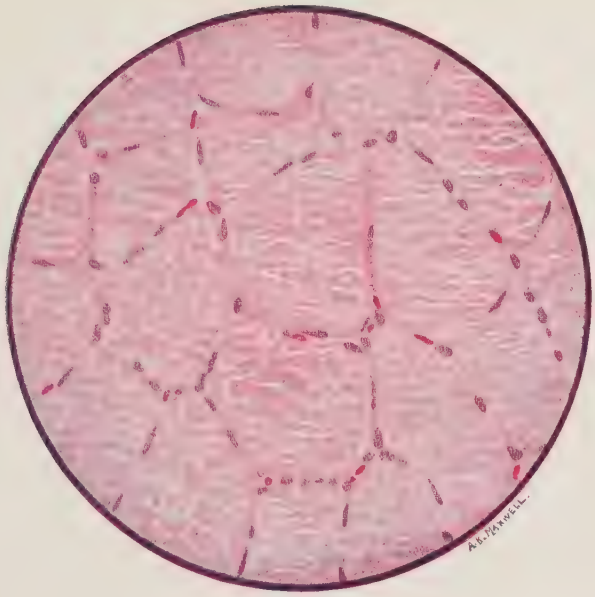

FIG. 1.—Gas gangrene. Normal muscle in transverse section, just beyond the edge of the spreading gangrene (British Medical Research Committee).

FIG. 2.—Gas gangrene. Muscle from as nearly as possible the visible advancing edge. Note the marked contrast between the dead coagulated fibers, which are separated off from their sheaths, and the paler normal fibers (British Medical Research Committee).

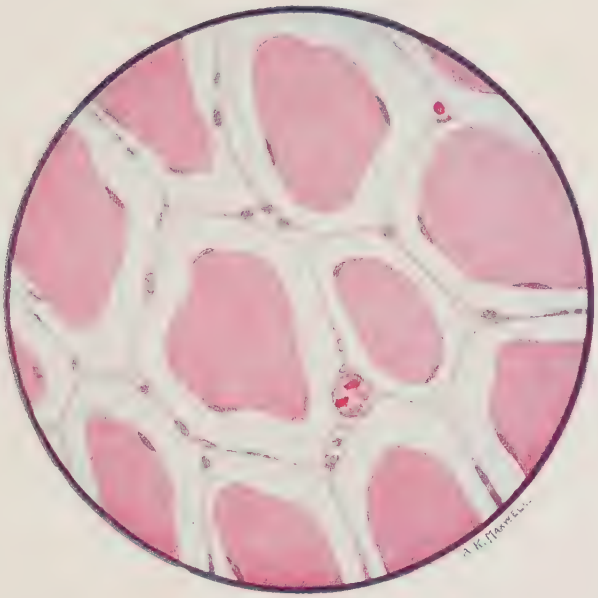

FIG. 1.—Gas gangrene. All the fibers are here degenerated, but their sarcolemmal nuclei still appear intact. Separation of the fibers from their sheaths is everywhere complete (British Medical Research Committee).

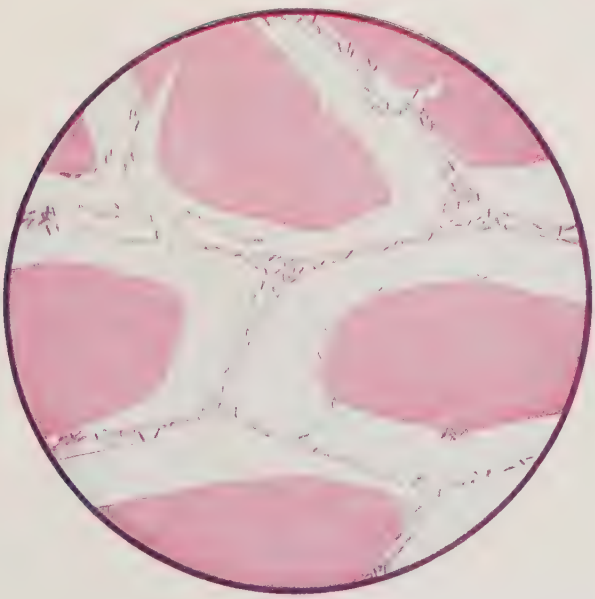

FIG. 2.—Gas gangrene. This shows the distribution of organisms at a comparatively early stage. There are large numbers of bacilli in the reticulum, but they have not yet invaded the fibers. This stage is slightly more advanced than that depicted in Fig. 1 and the nuclei of the sarcolemma have disappeared (British Medical Research Committee).

bacteria at the spreading edge are confined to the interstitial tissue and do not invade the muscle fibers. At a later stage the degenerating fibers are crowded with bacteria.

It would appear, therefore, that the bacilli spread up and down the muscle in the interstitial tissue, preceded perhaps by a toxic fluid which separates the muscle fibers from the interstitial tissue, and kills the fibers so that they may be invaded by the bacteria. It is thus easy to understand why the spread should be a longitudinal one, and why it should seldom occur in a transverse direction.

The toxins of the anërobic bacteria appear to be strongly antiphagocytic, and they inhibit the leucocytosis seen in the ordinary pyogenic infections.

Various *sera* have been used in the effort to combat gas gangrene. That of Bull of the Rockefeller Institute has given excellent results in the laboratory, but the reports of its effects when used in the field were so conflicting that no definite statement can be made as to its value. The same may be said of the other sera which have been tried.

Phagedena.—This condition, closely allied to or identical with hospital gangrene, is fortunately now so rare that little need be said on the subject. When it does occur now it is usually in connection with venereal sores. It is probably due to infection with anerobic organisms. The phagedenic ulcer is irregular in outline, but with sharply cut edges; the base is covered with a grey slough. The ulceration spreads rapidly as is the way with moist gangrene.

Cancrum Oris.—This fortunately rare form of gangrene occurs in debilitated children under the age of 5 years. It commences on the inner surface of the cheek or on the gums, and spreads until it has destroyed a large portion of the cheek and, it may be, of the bone. Death may occur from septic absorption or from bronchopneumonia.

References for Further Study

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CHAPTER V

HEALING

Two processes essential to the life and welfare of the organism are met with throughout the animal kingdom. The first of these is designed to counteract and offset the effects of an irritant upon the organism, and manifests itself in the various forms of inflammation. The object of the second is to make good the damage sustained in the onslaught of the irritant, and to reestablish in the tissues affected the former state of anatomical and physiological perfection. This kindly and beneficent process is known as healing or repair.

It is often taught that inflammation and repair are two phases of the same process, that repair, as it were, rounds off inflammation. Such a view is, however, hardly justifiable. Intense inflammation may occur without repair, as in pneumonia, and repair need not always be preceded by inflammation. Moreover the mechanism is quite different. In the process of inflammation the principal factors are the fluids of the blood and the wandering cells of the body, whether hematogenous or histogenous in origin. In healing, on the other hand, it is the fixed cells which are principally concerned, whether these are epithelial parenchymatous cells, vascular endothelium, or fibroblasts.

Although inflammation becomes more complex and probably more efficient as we ascend the animal scale, the reverse is true of healing. The latter becomes more complete the lower down we go, and in the lowest forms of life not only entire organs or parts may be replaced, but a complete new individual may be formed. The experiments of the Abbé Spallanzani in 1768 in this respect are classical. Working on the earth-worm he was able to obtain a new head five times in one animal. In man it is useless to look for the restoration of organs or parts. All that can be hoped for is a regeneration of tissues, and even this is limited in extent, and by no means shared by all the tissues. It is one of the penalties we have to pay for our aristocratic position in the animal hierarchy.

Moreover there is an aristocracy of tissue as well as of species. The more highly developed the tissue, the less power has it of regeneration. Comparatively lowly specialized tissues such as connective tissue, the periosteum, or the epidermis are readily regenerated. Highly specialized cells such as those of the heart or the central nervous system are not capable of regeneration. The difference is nicely seen in the case of a secreting gland, in which the somewhat plebian cubical epithelium of the duct can be reformed in a manner which is impossible for the more aristocratic columnar epithelium of the acinus.

Age bears an important relation to healing. The younger the animal the more complete is the healing. It was Spallanzani who long ago first pointed this out in his experiments on the tail of the tadpole and the limbs of the salamander.

Finally it must be borne in mind that, as Mallory has insisted, new cells are only formed in response to destruction of the same kind of cells. The fibrosis which occurs when part of the liver or the kidney is destroyed is not a proliferation of fibroblasts to compensate for the loss of liver cells, but is a direct response to destruction of the connective tissue itself. The proliferation of the more lowly organized tissue is always greatly in excess of that of a more specialized tissue, and therefore it appears to replace it—the so-called replacement fibrosis. When, however, the injury is wholly confined to the parenchymatous cells, as in focal necrosis of the liver, there is no response on the part of the connective tissue.

Much light on the subject of healing has been thrown within recent years by artificial tissue cultures *in vitro*. In such a culture fibroblasts can be seen sprouting out in all directions throughout the drop of plasma, although in reality probably following a thread of fibrin as it forms here and there. Epithelium, on the other hand, even when completely severed from its surroundings, grows as a solid sheet of cells just as it does when covering in a raw surface. Such characteristics of different cells may, therefore, be regarded as inherent peculiarities rather than as conditioned by the situation in which they happen to find themselves placed.

The recent work of Drew on the culture of tissues in a special saline medium of his own is of particular interest. Although considered more fully in the discussion of tumors (page 166) it may be briefly referred to here. Drew found that many of his tissue cultures reproduced with remarkable fidelity the tissue from which they were derived. The heart muscle cells pulsated, the epithelium of the breast of the pregnant animal secreted fat droplets which made the culture fluid milky, the renal cells arranged themselves in the form of tubules, and the skin epithelium showed cornification. The parenchymatous cells of an organ do not display their special characteristics in pure culture, but only when connective tissue cells have been added to the culture; it is only then that renal tubules are formed and squamous epithelium becomes cornified.

Another recent contribution to the subject of healing of great interest is that of Carrel. He has shown by means of tissue cultures that epithelium and fibroblasts do not build up their protoplasm in blood plasma or serum, but only do so when cultivated in the presence of embryonic tissue juices or lymphocytes. Lymphocytes, on the other hand, die when placed in embryonic tissue juices, but grow well in diluted serum. They can therefore obtain nourishment from the serum, whereas the epithelial cells and fibroblasts are unable to do so. Moreover Carrel considers that the lymphocytes have the power of liberating these nutritive and growth-producing substances, which he

calls *trephones*, into the blood plasma and the lymph spaces, and thus pass them on to epithelium and connective tissue; they act as mobile unicellular glands or "nursing cells" for these tissues. A similar effect can be produced *in vivo*, for fibroblasts show active growth in the presence of a peritoneal exudate or ascitic fluid containing many lymphocytes.

After this brief review of the general principles involved in healing, the process will be considered as it manifests itself in the individual tissues.

Healing of Wounds of the Skin.—From the surgical standpoint by far the most important example of healing is that afforded by wounds of the skin, whether accidental or the result of operative precedure. The process differs very materially, depending upon whether the wounded surfaces are in apposition or whether the wound is an open one. In the former the healing is primary or by "first intention;" in the latter it is secondary through the intermediary of granulation tissue, and is known as healing by "second intention."

Healing in an Incised Wound.—The passage of the knife produces two immediate results: (1) destruction of the cells in its path, and (2) opening of a number of blood vessels and lymphatics.

The tissues, both epithelial and fibrous, are killed as the direct result of the trauma. In experimental wounds necrosis may be observed by the end of the first hour. Blood and lymph are poured out in abundance between the cut edges, and soon the space is filled with a clot consisting of fibrin, leucocytes, and red blood cells. The hemorrhage ceases owing to the occurrence of thrombosis.

By the end of 12 *hours* inflammatory phenomena have begun to make their appearance, due partly to the trauma, partly to the irritation produced by the necrosed tissue and the clot. The vascular endothelium and the connective tissue cells on either side exhibit mitosis, and endothelial buds and fibroblasts begin to invade the clot. The endothelial buds originate as solid protoplasmic masses from the neighboring vessels, which first become longitudinally segmented and then canalized so as to admit the blood. The new vessels thus formed unite to form an anastamosing network. By the end of the *second day* we can see the familiar vascular connective tissue we know as granulation tissue, the development of which has already been fully considered in the chapter on inflammation (see p. 57). For the production of granulation tissue, therefore, it is by no means necessary to have the ordinary granulations of an open wound. It is the sine qua non of the healing of any wound. Phagocytic mononuclear leucocytes are busy devouring the fibrin. The surface epithelium shows evidence of regeneration in the shape of mitotic figures.

By the end of the *fourth day* the temporary clot has been entirely replaced by granulation tissue, the fibroblasts of which can be seen sewing the edges together. The squamous epithelium has covered over the narrow wound on the surface.

By the end of *three weeks* fibrosis has advanced so far, owing to the fibroblasts laying down collagen fibrils in their peripheral parts, that dense non-vascular scar tissue is formed, contraction of which leads to the usual depressed white surface scar. There may be an attempt at regeneration of the sweat glands in the deeper parts, but, as we have already seen, it is the cubical cells lining the ducts which

Fig. 11.—Repair of penetrating corneal wound by fibrin and leukocytes. The epithelium has extended over the anterior surface. (After Ranvier.)

are most likely to be successful in the effort, the acini themselves not being reformed. The scar, therefore, is without sweat and hair.

Healing in an Open Wound.—When there is a gap of some size in the surface it is evident that healing cannot occur by a simple sewing together of the opposing edges. The gap has now to be filled up gradually from below by the formation of a new tissue, and when the time is ripe the surface is covered over by ingrowth of the epithelium.

Although this process may appear at first sight very different from that which has just been described, in fundamentals it is exactly the same.

At first the surface is covered by a layer of inflammatory exudate consisting mainly of fibrin. Under this covering granulation tissue is formed, and it now presents the classical appearance of granulations visible to the naked eye. By the end of the *second day* minute reddish granules can be seen on the surface, which, increasing in size, give to it a characteristic granular appearance. They are made up of the vascular connective tissue already described, and bleed readily from

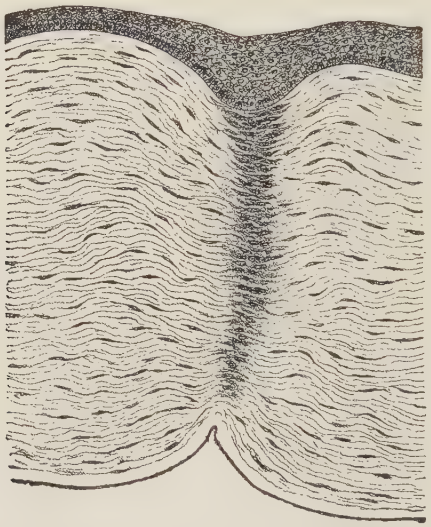

Fig. 12.—Healed wound in rabbit's cornea. Two weeks after injury. A slight opacity is noted on examining the cornea, due to the connective-tissue cells seen in the line of the scar. (Keen's Surgery, Vol. I.)

their thin-walled blood vessels. The granularity is due to a series of capillary loops which arch forward into the investing fibrin, and are supported by more or less connective tissue.

The granulating surface is covered by a thin sero-purulent discharge containing leucocytes and mononuclears. The amount and character of this discharge depend largely on whether or not infection is present. If the wound is quite clean it will be comparatively slight. If, on the other hand, it becomes infected the discharge will be abundant and frankly purulent.

The nature of the granulations also varies. In a healthy wound they are small, red, and firm. When the local conditions are unfavorable, either because of infection or from unsatisfactory vascular arrangements, the granulations may become large, pale, flabby, and

exuberant, and until these conditions are removed healing will not continue. Tuberculous granulation tissue presents this flabby unhealthy appearance to a very marked degree.

The microscopic character of the granulations depend very largely upon the presence of infection. If none is present the picture is one of a young vascular cellular connective tissue containing a few wandering cells, but composed essentially of fixed connective tissue elements. Should the wound be an infected one, this new tissue will contain in addition the elements of an inflammatory exudate. The cells and fibers are separated by inflammatory edema. In acute infections polymorphonuclear leucocytes are present in large amount. In chronic infections, tuberculosis, syphilis etc., the principal elements of the exudate are those wandering tissue cells which Maximow terms polyblasts, in which are included small round cells, large mononuclears, and plasma cells. For a discussion of these the reader is referred to the chapter on inflammation.

The cavity is steadily filled up from below by the granulations, which are progressively becoming organized until finally a patch of new tissue repairs the break in the surface. The surface epithelium commences to proliferate after two or three days, and a delicate bluish film can be seen creeping in over the red granulating surface, much in the same way as the first filaments of ice extend over a pond on an autumn evening. It is not, however, until the surface is in a perfectly healthy condition that regeneration of the epithelium need be looked for. As long as sepsis is present, none will occur. The ingrowing epithelial cells often project downwards, and send little groups of cells down between the capillary tufts, thus anchoring the film to the surface. The time occupied by the epithelium in covering a granulating surface varies greatly, depending upon the size of the area, the presence of infection, and other minor factors.

This method of secondary healing or healing by granulation tissue is by no means confined to the filling of a gap on the surface. It is the means whereby any cavity in the tissues becomes filled, although the attempt is not always successful. The cavity is occupied by blood or an inflammatory exudate, which is gradually replaced by granulation tissue. Even an abscess cavity is filled up in this way after the pus has been allowed to escape. A cavity in bone containing blood may fail to be obliterated, owing to the comparatively non-vascular character of the tissue, and for years may remain in this condition, full of fluid autolyzed blood, and a constant menace to the patient from the danger of infection supervening.

Healing under a Crust.—This is merely a modification of secondary healing. If there has been a good deal of hemorrhage a blood clot will form on the surface, which, if allowed to remain, will act as a protective covering under which healing will proceed quietly and unobtrusively. The same is true for the scab or crust which forms when the discharge from the surface of the wound is allowed to dry. This crust subserves the three-fold function of a protection, a scaf-

folding for the support of the young connective tissue, and a source of nourishment for the same.

The distinguishing feature of this form of healing is that the new epithelium extends over the surface under cover of the crust, so that when the latter drops off the raw surface is completely covered. Although there is plenty of granulation tissue under the epithelium, the patient escapes the discomfort of a raw granulating surface.

Healing in Epithelium.—Epithelium illustrates very well the truth that cells are only replaced by cells of the same kind. The appearance of an isolated island of epithelium in the center of a granulating area was for long considered an indication that the granulation tissue itself could give rise to new epithelium. It is now known that such instances are due to cells being accidentally carried in from the surrounding epithelium, or to the persistence in the ulcer of remnants of sweat and sebaceous glands.

The regenerative power of epithelium is very marked. Indeed in the skin and the alimentary canal a process of renewal is constantly going on. It is for this reason that skin-grafting is successful in so many instances. The process can best be studied in a superficial wound of the skin. Within a couple of hours signs of activity may be observed in the deeper layers of the epidermis at the edge. The cells in that region become detached and appear to glide over one another towards the area to be covered, so that presently the epithelium at the edge becomes thinner than formerly, being spread out, as it were, over a greater surface. By the end of 48 hours mitosis is in full swing, so that multiplication as well as translation of the cells is taking place. A thin bluish film creeps over the raw surface, many of the cells growing down in little clumps so as to anchor the film to the surface. As is but natural, it is the cells of the deeper layers, not those already cornified, which take part in the process.

Should anything interfere with the onward march of the epithelium, as in chronic inflammation and in tuberculous and syphilitic ulcers, the thwarted epithelium may send long processes down into the cutis vera, which may become snared off and form epithelial pearls. The appearance so closely resembles that of an early epithelioma that the differentiation may be a matter of great difficulty. Indeed such chronic ulcers may form the starting point of a malignant growth.

If the glands of the skin, both sweat and sebaceous, and the hair follicles have been completely destroyed they will not be reformed from the surface epithelium. If part of these deeper structures have been spared, a more or less successful attempt at regeneration may take place.

Healing in Connective Tissue.—Regeneration occurs even more readily in connective tissue than in epithelium. Moreover it is peculiarly resistant to destructive agencies, so that whilst the more highly specialized cells of an organ may be completely destroyed, remnants of connective tissue remain from which new fibrous tissue is formed, a condition of replacement fibrosis which is more apparent than real. If, as occasionally happens, the parenchymatous cells of the organ are

destroyed and the connective tissue spared, no replacement fibrosis will occur. In a burn of the skin the amount of scarring depends directly upon the amount of connective tissue destroyed.

The cells of white fibrous tissue are elongated, scanty in cytoplasm, and possess branching processes which are lost in the surrounding fibers. Shortly after injury these cells commence to proliferate. The cell becomes shorter and stouter, the cytoplasm is more abundant, and the large vesicular nucleus serves to distinguish it from wandering mononuclear cells. Division occurs, and the new cells put forth branching processes. The typical fibroblast, the former of new connective tissue, is readily recognized, but the shorter more rounded forms are less easily differentiated.

In the marginal part of the cytoplasm fibrils are laid down, which gradually become separated from the parent cells, and are arranged in parallel fashion to form wavy bundles of white collagen fibers. The fibroblasts lose their plump form, and, squeezed in between the fibrous bundles, revert to the narrow, elongated connective tissue cells which appear in sections to be little more than nuclei.

Healing in Elastic Tissue.—Elastic fibers are reformed very slowly, but abundant regeneration may in time occur not only in ordinary connective tissue, but especially in those situations such as the lung and the arteries where elastic tissue plays an important part. The exact method of regeneration is uncertain, but the fibers seem to develop as cellular processes from cells which cannot be distinguished from those which form collagen fibers. It is most probable, however, that these cells are in reality distinct, a point which can only be decided when we have finer technical methods at our disposal.

Healing in Fat.—The fat-cell is a specialized mesodermal cell which arises early in development. It is not a fibroblast, nor does it arise from one. At first it resembles a liver cell, with abundant granular cytoplasm and a central nucleus. Fine droplets of fat appear in the cytoplasm, and fuse into larger ones, but still leaving the nucleus centrally placed. Such cells, which are common in the lower animals, are occasionally found in the retroperitoneal fat in man. Finally the droplets fuse into one large globule, the nucleus is displaced to the side and flattened, and the cell assumes its characteristic spherical or polygonal shape.

In wasting the fat becomes replaced in the cell by fluid. In healed wounds of adipose tissue, as in the abdominal wall, evidence of regeneration may be seen, although much of the fat may be transformed into mucoid tissue. Within the empty fat-cells at the site of injury a number of smaller cells with finely vacuolated cytoplasm may be seen to develop. These probably represent regenerating fat cells which proceed to full development just as in embryonic life. There is, however, still considerable doubt regarding the whole subject of the repair of fat.

Healing in Cartilage.—Cartilage is such a non-vascular structure that healing is extremely slow. Moreover, when the damage is at all

extensive the defect is merely patched by fibrous tissue, the proliferative power of the cartilage being very limited.

Healing may take place in two ways: (1) through the activity of the perichondrium, and (2) by direct union.

The first method is that employed when the gap to be filled is of any size. The perichondrium is separated from the cartilage by blood or inflammatory exudate, and the space becomes filled with fibrin. The deep cells of the perichondrium proliferate and develop into fibroblasts which invade the fibrin. In course of time they become rounded and develop a capsule, and the matrix in which they lie becomes fibrillar, so that a fibro-cartilage has been formed. If the gap is large much of it will be filled with ordinary fibrous tissue.

The second method is seen in narrow incised wounds. The cartilage cells in the edges appear to multiply, and the matrix in their immediate vicinity may become hyaline or fibrillar. The edges are glued together, but without any of the phenomena of inflammation or the formation of granulation tissue. The healing of cartilage may take from three to six weeks.

The ultimate result depends much upon the use to which the new tissue is put. In excision of a joint, for instance, the new connective tissue covering the ends of the bones will, if movement be maintained, be converted into cartilage. If, on the other hand, an articular surface is not exposed to pressure the cartilage will revert to fibrous tissue. This is exemplified by such a deformity as club foot.

Healing in Bone.—The process of healing in bone is the same whether the injury is due to a fracture or to removal of some of the bone at a surgical operation. The changes leading to the union of a fracture may conveniently be considered.

As the result of tearing of the periosteum and the surrounding tissues blood is poured out, a certain amount of inflammation occurs, and a mixture of blood clot and inflammatory exudate is formed around and between the broken ends of bone. The amount of this exudate, which will determine the amount of subsequent callus formation, is dependent largely upon the accuracy of apposition of the two fragments. If little or no space is left and the line of the fragments is good there will be a minimum of exudate. If the gap is large, or the fragments override one another the exudate will be correspondingly bulky.

Healing of the fracture does not occur through the proliferation of the bone cells, for these are end products and are unable to multiply. It is accomplished by the formation between and around the ends of a temporary connective tissue of callus, which eventually becomes converted into true bone. It used to be thought that this new tissue was laid down by the periosteum. The work of Macewen, confirmed later by that of Gallie and Robertson, has shown that the osteoblasts belong to the cortical areas of the bone and not to the periosteum. If the periosteum be removed from a bone, and an experimental fracture be then produced, the formation of callus will be even more abundant than

under ordinary conditions. This question is discussed more fully on page 691.

The deeper layers of the periosteum soon exhibit inflammatory changes, leucocytes migrate from the vessels into the clot, and by the end of 48 hours the clot is pervaded by osteoblasts derived from the depths of the periosteum and by new capillaries. These osteoblasts are merely fibroblasts with the capacity of forming bone. At this stage, therefore, the intervening substance is ordinary granulation tissue.

In the course of four or five days this becomes converted into *osteoid tissue*, which is tissue resembling bone in its structural arrangement with a homogenous matrix but not possessing any lime salts. The osteoid tissue is scattered here and there in little clumps, and in the intervening spaces marrow-like tissue develops. Finally lime salts are laid down, and the ends are knit together by fully formed bone.

Part of the new bone may first be formed through cartilage. Areas of cartilage are laid down by the osteogenic tissue of the periosteum, and these are invaded by new vessels, converted into osteoid tissue, and finally calcified, just as happens in the normal development of bone in cartilage. This method of healing occurs where a large gap has to be filled up, and where there is a considerable amount of movement.

The healing of fractures may be interfered with in a number of ways. Sepsis, which is so often present in a compound fracture, always causes great delay. Fragments of muscle, fascia, or fat may intervene between the two fragments. Wide separation of the fragments renders the process of healing a long one, and the resulting union insecure. Some of the constitutional conditions referred to at the commencement of this chapter may interfere with healing. In all such cases the bond of union, if it occurs at all, is apt to be fibrous or cartilaginous rather than osseous, and the limb is unable to sustain any strain.

The mass of new tissue formed at the seat of a fracture is known as *callus* on account of its hardness. The fracture may be external, ensheathing the broken ends as a plumber's solder ensheaths a junction of pipes; intermediate, forming a direct union between the fractured surfaces; and internal, filling up the narrow cavity. The intermediate callus is the only form which persists. The internal and the external callus are in due time removed.

For the process of healing is by no means finished when the gap is patched and the ends united. A slow process of moulding ensues which may last for years. The removal of the internal and external callus is undertaken by large multinucleated cells known as osteoblasts, and this work is done so efficiently that it may be impossible to detect the site of the fracture. But for a long time afterwards a process of internal adjustment goes on whereby the somewhat haphazard preliminary arrangement of the bone lamellæ becomes moulded so that it conforms to the stresses and strains to which the part is subjected.

Healing in Muscle.—*Plain muscle* is incapable of regeneration. It is true that some of the cells may show mitosis, but no new fibres are formed. Union is due entirely to the formation of fibrous tissue.

The same is true for *heart muscle.* In spite of the presence of mitoses the union is fibrous and not muscular.

Striated muscle is capable of greater regeneration. Small incised wounds, especially if these are in the long axis of the muscle, may be healed so completely that no trace of scar tissue can be detected. Of course if a muscle fibre—which is merely a multinucleated mass of differentiated protoplasm—is completely destroyed no regeneration is possible. If, however, the destruction is only partial the remaining nuclei under the sarcolemma may enlarge and multiply, whilst around them there collects a mass of granular cytoplasm, so that sarcoblasts are formed. Longitudinal fibrils appear in the cytoplasm; these become transversely striated, and a new muscle fiber results. This process can be studied to best advantage in Zenker's degeneration in typhoid fever, where part of the fibre becomes necrosed and absorbed but the sarcolemma remains intact, and the development of sarcoblasts can be watched in the empty sheath.

When the wound is larger, and especially when it is across the long axis of the muscle, the divided fibers retract and repair is less efficient. In such a case a bulbous swelling can often be observed at the cut end of the fiber, consisting of a mass of protoplasm containing large numbers of nuclei. No new fibers are formed, so that although there is an increase in bulk there is no true healing by muscular tissue.

When the destruction of muscle is at all extensive the divided ends are separated by a large blood clot, and are finally united by ordinary scar tissue. Such union, although incomplete anatomically, is often physiologically quite efficient, but there is always a danger that the scar may stretch.

Healing in Tendon.—The repair of tendon is of considerable importance, not only because of occasional division as the result of accidents, but more especially because of the common operation in orthopedic surgery of the transplantation of tendons.

In spite of the fact that a tendon is practically non-vascular, the healing which it undergoes is usually very complete, not only functionally as in muscle, but also anatomically. The usual inflammatory phenomena associated with repair are lacking, owing to the absence of blood vessels.

When a tendon is divided the ends retract, and the intervening space is filled with blood clot. The clot is replaced by two varieties of cell: (1) fibroblasts derived from the connective tissue sheath, which show mitosis at the end of the second day; (2) tendon cells which can be seen proliferating by the end of the fourth day. The proportion of these two depends on local conditions. If the gap be small and asepsis complete the union may be largely tendinous; if the reverse be the case it will consist of scar tissue.

The healing of tendon is a slow process. Under the most favorable conditions it will occupy two weeks, and it may take over two months, especially if the wound becomes infected. Sepsis greatly retards the process, because necrosis occurs so readily in the non-vascular tendon.

Any excess of patch tissue is usually absorbed, but occasionally adhesions develop between the tendon and the synovial sheath which greatly interfere with the subsequent movements.

Healing of the Serous Membranes: Adhesions.—The serous membranes such as the pleura, the pericardium, and the peritoneum may be wounded by missiles or injured in the course of an operation, but of even greater interest is the injury produced by inflammation.

The injured surface is covered by a layer of fibrin or inflammatory exudate, the fibroblasts of the subserous connective tissue proliferate and invade this layer, blood vessels grow in, granulation tissue is formed, organization occurs, and the epithelial cells rapidly creep over the mass and cover it. A slight thickening and opacity may be all that remains to indicate the seat of the injury, and even that may be lacking.

Adhesions.—When two injured or inflamed serous surfaces are in apposition adhesions between them are certain to form. In the abdomen even a very slight amount of trauma is sufficient to lead to adhesions, so that the bowel or the omentum will usually be found adherent to the incision in the abdominal wall. Adhesions form with remarkable rapidity. At the end of an hour some force may have to be exercised to separate the two surfaces, by the end of two days there is firm union, and by the sixth day healing is complete.

When the adherent surfaces are separated it is seen that they have lost their normal glistening appearance and are quite pink. There may be petechial hemorrhages under the serosa. The epithelium may be absent. Often, however, this layer is still present, but the cells are extremely swollen and very irregular. The adhesions, at first mainly fibrinous, rapidly become converted into granulation and finally fibrous tissue. The fibrous adhesions become covered with a lining of epithelium. The movements of the bowel may draw the adhesions out into long strings. The adhesions, although usually permanent, may in some cases be absorbed. An abdomen which when opened is full of adhesions may at a second laparotomy be found to be almost free.

Healing in Mucous Membranes.—The principles already studied in the healing of skin wounds apply to mucous membranes, but with slight differences. The surface epithelium is rapidly and completely regenerated by the dual process of migration and proliferation already described. We have seen that in the skin the specialized glands and hair follicles are not regenerated at all from the surface, and only imperfectly from portions of the glands which may have escaped injury. The much simpler tubular glands of the stomach and intestine are more readily replaced from the surface epithelium, but repair is much more complete if remnants of the glands still persist and take part in the process of regeneration.

Repair in the gall bladder, urinary bladder, and ureters proceeds on similar lines. If the muscular coat is injured in addition, that portion of the wall will be replaced by scar tissue, following the principles already discussed.

In the uterus repair of the endometrium goes on after each menstrual period, and on an extensive scale after pregnancy. After curettage the surface is rapidly regenerated, the glands being reformed from those tubules which penetrate the muscularis and thus escape removal during the operation.

The extensive destruction at the placental site is repaired in a similar manner.

Healing in the Liver.—Wounds of the liver are repaired by scar tissue. A certain amount of proliferation of liver cells takes place, but they do not take a prominent share in the healing process.

Much more marked evidence of regeneration is seen in destructive processes such as cirrhosis and acute yellow atrophy. A large number of new bile ducts appear, although it is possible, as Milne has suggested, that this appearance is merely due to an enlargement of pre-existing minute ducts. These new ducts may be seen to be connected with masses of liver cells, which have been supposed to have originated from the ducts. It is more probable, however, that the ducts are making communications with the old liver cells, and that the new cells which are undoubtedly formed are derived only from liver cells.

Healing in the Kidney.—In considering the subject of kidney repair it is necessary to differentiate the enlargement of one kidney following removal of the other from a true regeneration after injury. The former is merely a compensatory hyperplasia in which the cells increase in size rather than multiply in number.

The specialized convoluted tubules and glomeruli are not regenerated after an injury, although the cells of the more lowly connecting tubules are able to multiply and form new tubules, an example of the penalty to be paid for high specialization. In acute nephritis, however, if some of the epithelial cells are destroyed they may be replaced by multiplication of the other cells of the tubule.

Repair following wounds of the kidney is of particular interest in view of the frequency with which the organ is incised in the search for stone, tuberculosis, etc. From what has just been said it is evident that healing of a wound can only take place through granulation tissue and scar formation, although the collecting tubules may make a feeble attempt at repair.

The amount of damage done depends largely upon the direction of the incision. The tissues in the immediate course of the incision are killed, but in addition those in the neighborhood may die if their blood supply be cut off. If the incision be made perpendicular to the convexity and thus parallel with the vessels this secondary effect is comparatively slight. When, however, it is made obliquely or at right angles to the transverse vascular arches a large more or less wedge-shaped area is deprived of blood, anemic necrosis results, and an infarct is produced. The kidney is an intricate and delicate mechanism, and the treatment it sometimes receives at the hands of the surgeon is apt to suggest an attempt to open a watch with a sledge-hammer.

Decapsulation of the kidney is a surgical proceedure recommended by Edebohls for the treatment of chronic nephritis, on the assumption that the increased vascularity consequent upon the ingrowth from the raw surface into the kidney would prove beneficial. Experimental work, however, has demonstrated the entire uselessness of the proceeding. It is true that new vessels grow into the substance of the kidney and anastomose with the renal vessels, but these are presently obliterated and cease to function. The new capsule which forms is much thicker and denser than the old one, as was only to be expected. Finally, the capsule is so adherent in chronic nephritis that it has to be forcibly torn off, and the injury to the cortex which results leads to necrosis and scarring, and still further aggravates the condition.

Healing in Nerves.—The repair of a nerve after injury became a question of paramount importance both during and after the recent war, owing to the frequency with which the peripheral nerves were divided.

When a peripheral nerve is cut the entire distal portion undergoes the changes first described by Augustus Waller in 1850, and now known as Wallerian degeneration. By distal portion we mean the part separated from the nerve cell from which it arises and from which it derives its nourishment.

In the case of a motor nerve whose trophic center is in the anterior horn of the spinal cord the degeneration extends down the nerve; in the case of a sensory nerve it may pass up or down, the former if the section is between the posterior root ganglion and the cord, the latter if it is distal to the ganglion. The degeneration also involves the proximal portion as far as the first node of Ranvier, or even a little further.

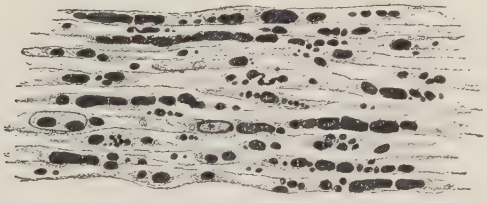

FIG. 13.—Section of a nerve forty-eight hours after injury. Fragmentation of the medullary sheath and axis-cylinder and the formation of myelin droplets are shown. Stained with osmic acid. (Keen's Surgery, Vol. I.)

Characteristic changes occur in the three structures of which the nerve is composed, namely the axis cylinder, the medullary sheath, and the neurolemma or nucleated sheath of Schwann. The *axis cylinder* becomes fibrillated and degenerated, no longer stains properly, and soon disappears. The *medullary sheath* becomes segmented and broken up into large masses of myelin, which soon give way to smaller globules staining black with osmic acid just like the normal medullary sheath. Both of these changes are well marked by the end of the

second day. In the course of a few weeks the myelin completely disappears, and the degenerated fibers can only be made out as clear spaces among surrounding healthy fibers stained blue-black by the Weigert medullary sheath stain. By the third day the nuclei of the *sheath of Schwann* begin to proliferate, they pass in between the myelin droplets, and collect around them a mass of cytoplasm in much the same way as do the sarcoblasts in regenerating muscle. The proliferated nuclei arrange themselves in long, tubular strands. Degeneration, therefore, is most intimately associated with regeneration.

For many years there has been acute controversy as to whether the regeneration is *peripheral*, the new fibers being laid down by the nuclei of the neurolemma and joining up later with the proximal end, or *central*, the fibers being formed as outgrowths from the divided central end. Although there have been distinguished supporters of the peripheral hypothesis, the central theory has won a conclusive victory. At the same time it is sometimes difficult to account for a speedy return of function on the hypothesis that the new fibers have grown from the site of the lesion to the motor or sensory end organ concerned.

Repair of a nerve, then, is due to the outgrowth of new fibres from the divided proximal end. In the course of a few days the axis cylinder begins to grow out in search of the missing distal end. It is not filiform, for a nodular mass of protoplasm has collected around the end, and new fibrils arise from this mass only when it reaches the distal end. Ross Harrison has made some very interesting observations on this process in the primitive nerve tube of the larval frog. He was able to demonstrate that the blunt end creeps forward by a kind of ameboid movement over the intervening space at the rate of one micromillimeter in 2 minutes. In man, if the space between the two ends be not greater than one inch, the advancing end will cover the distance. There are two factors which will prevent union: (1) the presence of scar tissue between the ends, and (2) a gap greater than can be covered by the regenerating proximal end.

When the bulbous end of the axis cylinder reaches the distal end it puts forth fine fibrils which probably grow down the tubular sheath formed by the nuclei of the sheath of Schwann.

If the distance is too great to be bridged or if the part supplied by the nerve has been amputated, the axis cylinders, frustrated in their attempt at reunion, may coil up so as to form a nodule, capped by fibrous tissue, at the end of the nerve. Such a mass, composed of nervous and fibrous tissue, is called a *stump neuroma*, but it is in no sense a true tumor.

The time necessary for the complete restoration of function, even when the cut ends have been brought into accurate apposition, is about three or four months. When the conditions are unfavorable it is considerably longer. Sensation usually reappears sooner than motor power. In cases of nerve grafting, where a nerve arising from

one nucleus may be connected up with one arising from another, it will be much longer before function is restored.

The Wallerian degeneration in the peripheral nerve is accompanied by a curious series of changes in the corresponding ganglion cells. These changes are known as *Nissl's degeneration*, because they particularly affect the Nissl substance in the cells.

Two or three days after nerve section the Nissl granules in the cell break up into very fine particles and ultimately disappear, the nucleus assumes a characteristically eccentric position, and the entire outline of the cell may disappear. Regeneration usually sets in by the end of three weeks, characterized by the reappearance of the granules and cell outline, and the resumption by the nucleus of its usual position. If the function of the nerve be permanently interfered with, as in the case of an amputation, there may be a secondary degeneration of the cell some months later, accompanied by complete atrophy and disappearance.

In the *central nervous system* no repair after injury occurs worthy of the name. The nerve cells are quite unable to regenerate. When the nerve fibers are injured, in the spinal cord for instance, there may be an ineffectual attempt at repair similar to that which occurs in the peripheral nerves, but it never comes to anything.

The only nervous tissue in the brain and cord with power of regenerating is the neuroglia. This is a connective tissue of epiblastic origin, the cells of which are capable of abundant proliferation. When the brain tissue is injured, necrosis, liquefaction, and absorption are apt to occur, and the gap is filled by neuroglia. Eventually, however, the ever-present fibrous tissue asserts itself, and the neuroglia forms only a narrow dense zone surrounded by fibrous tissue.

Healing in Blood Vessels.—When an artery or vein is cut or torn the break in the wall is repaired in a manner peculiar to the vessel. A sticky mass of blood platelets and fibrin forms in the gap, and this thrombus forms a temporary patch which is presently replaced by fibrous tissue. The whole process is considered in detail on page 137, so that it need not detain us longer here.

Healing in Non-vascular Tissue.—Examples of healing in non-vascular tissue have already been considered in the case of cartilage and tendon. The cornea, however, offers a peculiarly favorable opportunity for the study of healing uncomplicated by the vascular phenomena of inflammation.

If the wound passes through the epithelium, the connective tissue laminæ, and Descemet's membrane so as to open the anterior chamber the following changes will occur. An exudate is formed from the tissue spaces and from the aqueous humor which soon binds the two surfaces together in a fibrinous union. The connective tissue cells proliferate, invade the fibrinous clot, and organize it into the anterior part of the gap, and by the end of a week both it and Descemet's membrane are completely reformed.

It is, however, in superficial wounds involving only the corneal epithelium that the most avascular conditions are attained, for here no exudate of any kind is formed. The repair is carried out entirely by the epithelial cells. These first exhibit ameboid movement, move towards the wound, and begin to cover the surface. By the end of 12 hours they show mitotic division, and soon mitosis is in full swing, and the gap is covered by a layer of epithelium without any admixture of scar tissue and perfectly transparent.

Healing of Wounds in Tissues under the Best Conditions

Tissue	Degree of repair	Rate	Origin of new tissue
Epithelium	Complete.	Rapid.	Epithelial cells.
Connective tissue	Complete.	Rapid.	Fibroblasts.
Elastic tissue	Partial.	Very slow.	Elastic tissue cells.
Fat	Partial.	Slow.	Embryonic type of fat cell.
Cartilage	Partly cartilaginous, partly fibrous.	Very slow.	Perichondrium.
Bone	Complete.	Rapid.	Periosteum.
Plain muscle	Scar.		
Heart muscle	Scar.		
Striated muscle	Partial.	Slow.	Muscle fibers.
Tendon	Complete.	Very slow.	Tendon cells.
Mucous membrane	Complete.	Rapid.	Tubular glands.
Liver	Scar.		
Kidney	Scar.		
Peripheral nerve	Complete.	Very slow.	Axis cylinder.
Central nervous system	Scar.		
Cornea	Complete	Rapid.	Corneal cells.

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CHAPTER VI

TUBERCULOSIS

Tuberculosis, together with syphilis and the other infective granulomata, is usually regarded as a chronic inflammatory condition. We shall see, however, that in its purest form, namely when tubercle bacilli gain entrance to the body for the first time, the characteristic reaction is a proliferative one rather allied to tumor formation than an exudative reaction such as we associate with inflammation. It is only when the body has become altered by the residence within it of tubercle bacilli that it learns to react towards fresh invaders from without and from within in an inflammatory fashion.

Tuberculosis is the most important killing disease affecting mankind. It is responsible for no less than one-seventh of the deaths in the world. Owing to circumstances to be discussed presently the lungs are the organs which most frequently manifest the disease tuberculosis, but it is the lymphatic system which is *par excellence* the hunting ground of the tubercle bacillus. The disease may attack any tissue, but in addition to the lungs may be mentioned the lymphatic glands, the bones and joints, the spinal column, the brain, the eye, the intestine, the peritoneum, the Fallopian tube, the kidneys, bladder and testicle, and the skin. It is of interest to note that many of the organs specially prone is syphilitic infection such as the heart, blood vessels, pancreas, liver, and spinal cord are rarely the seat of gross tuberculous lesions.

The Tubercle Bacillus.—Tuberculosis is caused by the Bacillus tuberculosis, the discovery of which by Koch in 1882 served at once to establish the identity of a number of conditions such as lupus, Pott's disease, scrofula, and phthisis, which were previously regarded as quite distinct entities. The bacillus is a thin curved rod, from 3 to 4 μ in length, sometimes presenting a beaded appearance, staining with difficulty, and best shown owing to its acid-fast properties by the Ziehl-Neelsen method. It does not grow on ordinary media, but on glycerine-egg an abundant wrinkled growth makes its appearance after the lapse of two or three weeks.

The acid-fastness of the tubercle bacillus is due to the fatty envelope by which it is surrounded, and Dreyer has shown that this substance has a supremely important influence on the immunity reactions of the organism. An acid-fast organism resists digestion with trypsin, and therefore also digestion by the body fluids. The bacillus has little or no antigenic power because the specific bacterial proteins on which the immunity response depends cannot be liberated. When the fatty envelope has been removed the bacillus, now attenuated to

the thinness of the spirochæta pallida, displays active antigenic power. Dreyer has also shown that the severe local reaction with infiltration and sometimes necrosis which may follow the injection of dead tubercle bacilli is dependent on the irritation produced by these lipoid bodies and not to the specific antigenic proteins.

In culture the bacillus may show branching forms, suggesting a relationship with the streptothrix group, a group of which the Actinomyces bovis is the most important member.

There are two varieties of tubercle bacilli of importance in human pathology, the human and the bovine. Although Koch originally contended with the full weight of his authority that the human and bovine forms were so distinct that the bovine bacillus was unable to affect man, it is now generally admitted that the disease in man may be caused by either type, but that the bovine type is commoner in children owing to the larger amount of milk which they consume.

The two varieties of bacilli can not be differentiated with certainty on morphological grounds. They can readily be distinguished in culture and by animal inoculation. On glycerine agar the human type grows readily, the bovine not at all; the former is said to be eugonic, the latter dysgonic. Intravenous injection of a minimal dose of human tubercle bacilli in a rabbit will not result in death, whilst with the bovine type the animal will die of general miliary tuberculosis.

The disease in man may be caused by either type. Pulmonary tuberculosis in the adult is nearly always due to the human type. In children the bovine type is often the infecting organism, particularly in disease of bones and joints and of glands. The incidence appears to vary markedly in different localities, depending on the nature of the milk supply. In Edinburgh John Fraser found the bovine bacillus in 58 per cent of his cases of bone and joint tuberculosis in children, and in the same city Mitchell found that 90 per cent of the lymphatic gland tuberculosis in children was bovine in origin. Much lower figures are reported by workers in England and America. In 392 cases of bone and joint tuberculosis investigated by the British Royal Commission there were only 20 per cent of bovine infections, and the Imperial German Board of Health found only 5 bovine infections in 99 cases of all ages. The human type of bacillus is that responsible for most cases of bone and joint tuberculosis in the adult.

The fact that many cases of tuberculosis in children are due to the bovine type of bacillus, whilst in the adult nearly all the cases show the human type suggests the possibility of the mutation of one type into the other. Just as prolonged cultivation on special media may alter the characteristics of a microörganism, and passage through an animal body may enhance or diminish its virulence, so a lengthy sojourn in the human body may profoundly modify those features by which the bovine type of bacillus is distinguished. The evidence is not at present sufficient to decide this question.

Infection.—All tuberculosis is due to infection with the tubercle bacillus, but the problem of infection cannot be stated thus baldly.

It is not the bacillus alone which has to be considered. In every case there are two elements concerned, one destructive, but the other conservative. There is the seed, but there is also the soil. The seed, as Osler put it long ago, may fall by the wayside, or on stony ground, or among thorns, or finally it may fall on good ground and bring forth fruit an hundredfold. The seed of tuberculosis is so universal that it falls on practically all mankind, but fortunately a high natural or it may be an acquired racial immunity is so general that in most cases the soil remains barren, but for a healed tubercle here and there indicating the powers of defence. As we shall see, however, the term healed tubercle is not really justified. Although the active process may to all appearances have died out, and the lesion seems to consist of nothing but a mass of fibrous tissue, yet inoculation experiments will almost invariably reveal the presence of living tubercle bacilli.

Moreover, a fundamental distinction must be drawn between primary and secondary infection. From the evidence furnished by the autopsy room and by tuberculin tests we know that a large proportion of the population is infected by the tubercle bacillus before the age of puberty. But this does not imply that they are suffering from tuberculous disease. Tuberculosis as it occurs in adults is due to reinfection. The more or less chronic course pursued by the disease in adults is an indication that the patient has already been partially immunized in childhood. In peoples, such as those of remote and uncivilized countries, who have not had the benefit of this protective inoculation, tuberculosis spreads both amongst the population and throughout the body of the patient with the fury of one of the zymotic diseases.

The war has recently furnished two interesting examples of the truth that when members of an isolated community in which tuberculosis is rare are brought into contact with people amongst whom tuberculosis is common, they show an extreme degree of susceptibility to the disease.

The first example is taken from the western front. The South African Labor Corps unit, consisting of Kaffirs and Cape Boys, of an average strength of about 11,000, had more deaths from tuberculosis than had the whole of the British troops in France, of an average strength of 1,500,000. The actual figures in 1918 were 74 deaths amongst the British, and 113 deaths amongst the Kaffirs. The environment was the same for both, both were equally exposed to infection by the tubercle bacillus. The difference lay in the soil, which in the Kaffirs was virgin ground, but in the British had been transformed by repeated minimal infections in the early years of life.

The other example is provided by the inhabitants of Jerusalem. Two classes of Jews have returned after their exile of centuries. The first comprises the Jews scattered all over Europe and America, living in the most crowded districts of the great cities under the worst conceivable conditions, but with an acquired immunity so great that the disease has no terrors for them. There is universal tuberculous

infection but no tuberculous disease. The tuberculin test (von Pirquet) is positive. The second group is the Jews of the Yemen who have led an isolated nomadic life in the Arabian desert, and for centuries have been shielded from tuberculous infection. The tuberculin test is negative. These two groups of the same nation met in the streets of Jerusalem, and the result was disastrous to the Jews of the desert, for they acquired from their urban compatriots not only tuberculous infection but also tuberculous disease, and died off in large numbers.

The source of this secondary infection is still a vexed question. Is it exogenous or endogenous in origin? Does the infection come from an outside source, or is it supplied by the patient himself from within? In pulmonary tuberculosis and in the more purely surgical forms of the disease it is probable that the latter answer is the correct one. The recent increase in tuberculosis in countries where the entire population is suffering from undernutrition as the result of the war can hardly be due to a sudden increase in infection from without, and must be accounted for by the activation of a preëxisting focus within the body. In the last ten years no native of so great a tuberculosis center as Saranac Lake has died of pulmonary tuberculosis.

The natural resistance of the body comes to assume great importance in cases in which the tuberculous disease is secondary to a focus which keeps up a constant supply of infection. In tuberculosis of the bladder the condition is kept active by the passage of bacilli down the ureter from a tuberculous kidney, and tuberculous peritonitis in the female is frequently secondary to infection of the Fallopian tubes. In these cases if the primary source of infection in the kidney or tubes be removed, the secondary lesion will often look after itself.

Owing to a lowered resistance, however, the soil may become suitable. Such a low resistance may be congenital, transmitted, and familial; or it may be acquired from unsuitable environment, lack of nourishment, or the depressing effects of some other disease such as measles or influenza. A recognition of the importance of the soil is of great moment in matters of treatment, for though it be not possible to attack the bacillus by direct means, we may yet make the soil so unsuitable that a natural cure is effected.

Mode of Entrance.—Tuberculosis is above all a disease of the lymphatic system. But before the bacilli can gain entrance to that system they must pass through the epithelium of the skin or of a mucous membrane.

Direct infection through the skin is a very rare occurrence. A butcher handling tuberculous meat may be infected through a crack or wound of the skin. A pathologist may develop "post-mortem warts" or verruca necrogenica, a papular or pustular condition of the hands in which tubercle bacilli may be demonstrated. A hospital orderly may cut his hand with a broken sputum cup, and so become infected. But these are interesting because of their rarity.

It is through the mucous membranes, respiratory or alimentary, that infection usually occurs. Despite however the enormous amount

of attention which has been devoted to the subject, there is as yet no unanimity as to the most important method of infection in man. The inhalation directly into the lungs of the bacilli in dried sputum converted into dust, the similar inhalation of bacilli in droplets of sputum coughed directly from the mouth of a phthisical patient, the ingestion of tuberculous milk—all of these methods have their exponents, and it may well be that any of these may be the method of infection in a given case. Certainly experimental lesions can be produced in animals by any of these methods. The difficulty is to determine the common mode of infection in man.

It is usually assumed that the choice must be made between one of two main routes, namely the ingestion of tuberculous milk and the inhalation of tubercle bacilli either in dust or suspended in droplets of sputum. Both of these may be described as domestic methods of infection; the infection is acquired in the home. But Krause has drawn attention to the interesting fact that of the 75 per cent or more of persons who became infected with tuberculosis before adolescence, more than half are infected for the first time during the three years between the ages of three and six, whilst in the first three years of life only one-quarter are infected.

Now it is during these first three years that the child is brought into closest contact with the two incriminated sources of infection—the phthisical patient and tuberculous milk. During the second three years, the years of highest infectivity, he leads a more purely outdoor life than at any subsequent period. During this time he is continually contaminating his hands with the tuberculous sputum of the highways and the floors of houses, and as constantly conveying this material to his mouth. As Krause puts it, we live at present in a world of sputum, and the chances of infection are so great that few can escape. It is possible, therefore, that crude human sputum may play a much more important part in infection than either the dust or droplet theories would lead one to believe.

There can be little or no doubt that it is through the alimentary canal that the tubercle bacillus gains entrance to the lymphatic system, the principal portal being the nasopharynx and the small intestine. In the pharynx the tonsils stand on guard like Scylla and Charybdis to arrest unwelcome bodies from passing onwards. Weller, Crowe, and other observers have shown the remarkable frequency with which tubercle bacilli can be demonstrated in tonsils which show no gross evidence of tuberculous infection. The incidence of this infection is at least 5 per cent, and probably a good deal higher. Large numbers of tubercle bacilli must thus gain an entrance into the lymphoid tissue of the pharynx, and from what has just been said it is evident that these bacilli may be of the human as well as of the bovine type.

In the intestine, as Calmette repeats with such emphasis, the door is also flung wide open. The function of the small intestine is one of absorption. After a meal bacteria may be demonstrated in the chyle, the mesenteric glands, the lymph of the thoracic duct, the blood, and

even in the viscera of experimental animals, but not in fasting animals. The tubercle bacillus, once it has reached the small bowel, has little difficulty in traversing the epithelium and reaching the lymphoid tissue. Indeed the Peyer's patches may be regarded as lymphatic sponges through which wandering cells may readily pass between the cells of the epithelium.

Let us trace the possible course of a tubercle bacillus once it has started on its Odyssey. At the very outset it must be recalled that the bacillus is not motile. If it is to be moved from one place to another it must be transported passively. The two chief means of conveyance are phagocytic cells and the blood stream.

When the bacillus settles upon the mucous membrane of the nasopharynx or the small intestine it is engulfed by a phagocytic cell, usually a polymorphonuclear, which carries it by virtue of its ameboid movement between the lining epithelial cells into the tissue spaces and thence by way of lymphatic channels to the lymph glands which drain the part. Here it may settle down and multiply. If it succeeds in passing this barrier it will be carried into ever larger lymphatics till it reaches the thoracic duct and thus the blood stream. Its course is thus always centripetal. Carried by the blood to the right side of the heart the swollen phagocyte which contains it and the many other bacilli to which by this time it has given rise is filtered out by the pulmonary capillaries. It does not remain within the capillary, but is carried through the wall by its phagocytic host, and soon comes to lie in the adventitial lymph spaces. Having thus reentered the lymphatic system, it is again drained centralwards towards the tracheobronchial glands, or, if it succeeds in passing these it may once more enter the blood stream. Those bacilli which are not filtered out in the lungs will gain the left side of the heart, and may thus reach any organ in the body by way of the systemic circulation.

It will be seen that in most cases the portal of entry will defy detection. Once the door is closed there is nothing to show that the bacilli have passed through it. Only in those cases where the infecting dose has been unusually large will a lesion in the sentinel gland indicate the site of the initial infection. As a rule the first symptoms will be due to lesions in an organ far removed from this original site. Thus Cohnheim's idea that the primary localization depends upon the portal of entry can no longer be entertained. The infection remains latent for a varying period in the blood or the lymph stream, the development of the primary lesion depending largely on anatomical conditions. One of the best demonstrations of the silent entrance of tuberculosis into the body is afforded by the experiments of Calmette on the eye of the guinea-pig. Tuberculous sputum placed in the eye will produce tuberculosis of the cervical and bronchial glands without the slightest lesion in the eye itself.

From this brief outline it is evident: (1) that the most certain evidence of tuberculosis will be found in the lymphatic system, (2) that the lungs are of all organs the most likely to become involved, and (3)

that any tissue in the body may undergo quiet and unobtrusive hematogenous infection from some lymphoid lesion which may never be discovered. Tubercle bacillus bacillemia is common in all forms of tuberculosis. Indeed Rumpf found tubercle bacilli in the blood in 100 per cent of 25 patients whom he examined.

It may appear remarkable that the bacillus should remain viable and unharmed for such long periods within the bodies of phagocytic cells which so readily destroy other bacteria. The reason is that the tubercle bacillus is protected by its lipoid envelope upon which the proteolytic ferments of the phagocyte are unable to make any impression. It is to this lipoid substance that most of the local effects of tuberculosis are due; it is to the essential protein of the bacillus, liberated by the destruction of the bacillary bodies, that we must ascribe the allergy or hypersensitiveness which plays so important a part in the development of the disease.

The Miliary Tubercle.—However varied may be the pathological manifestations of the tuberculous process, the initial lesion is almost always the miliary tubercle, although occasionally we meet with a more diffuse reaction, the tuberculous granulation tissue. The early stages in the development of the tubercle are best observed in the experimental animal, but it must be borne in mind that the response of the tissues to tuberculous infection may be very different in the tubercle-free animal from that which occurs in an already tuberculous animal, the latter, of course, being the type of lesion observed in human pathology.

Two types of reaction are met with in tuberculous lesions. The first is a pure cellular proliferation, and is neoplastic in type; the second is represented by an outpouring of leucocytes and serum, and is exudative or inflammatory in character. The pure and characteristic reaction to tuberculous infection for the first time, provided that the infection is not too heavy, is a proliferation of the cells of the part—not the parenchymatous cells, but cells which are probably endothelial in origin and line the adventitial and other lymph spaces. The cells are larger than a leucocyte, and possess a large vesicular nucleus and a clear cell body with processes which may anastomose with those of its neighbors, thus giving rise to an apparent reticulum. It is to these cells that the name epitheloid is applied, but they bear no relation to epithelium. The reticulum is known as the *endothelial reticulum*. A small mass of pale-staining tissue is thus formed which becomes visible to the naked eye as a tiny grey translucent nodule at about the end of the second week, and is then known as a *miliary tubercle* from its approximation in size to that of a millet seed. A clump of bacilli may be demonstrated in the middle of the tubercle.

In addition to the endothelial cells one or more cells many times the size of their fellows may be seen situated usually towards the center but occasionally at the periphery of the tubercle. These cells contain many nuclei, often twenty or more, which are characteristically grouped at one or other pole or arranged around the periphery, although

a few may be found in the center. These cells are true foreign body *giant-cells*, and usually contain tubercle bacilli. They are apparently formed by the fusion of a number of endothelial cells, and it is probable that both types of cell represent a reaction against the fatty and waxy envelope of the bacilli, which cause them to be treated as foreign bodies. Whilst giant cells are very characteristic of tuberculosis, they are found in other chronic inflammations such as syphilis and actinomycosis; they are also seen clustered around foreign bodies in the tissues such as a piece of a silk suture, tiny particles of bone, etc.

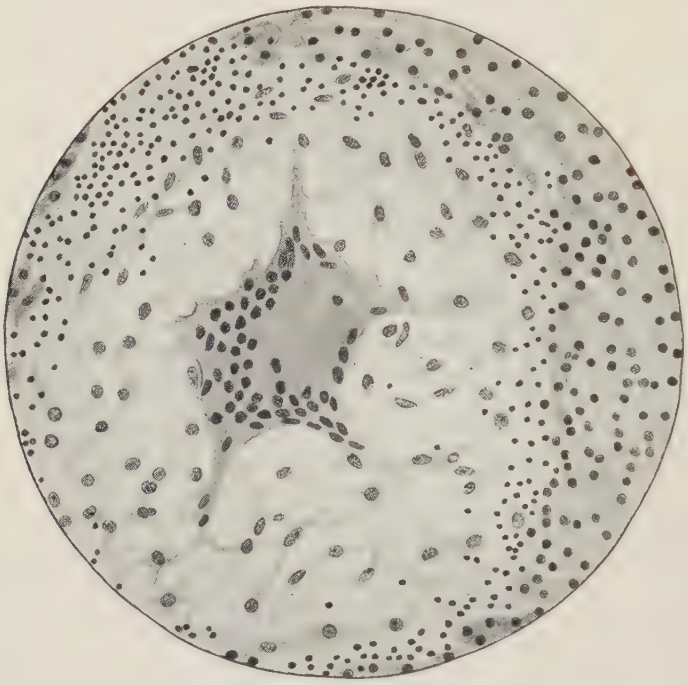

FIG. 14.—A miliary tubercle in the liver, showing a central giant cell, the endothelial reticulum, and a narrow zone of lymphocytes.

Moreover they may be absent from tuberculous tissue. Tuberculosis sometimes takes a slow and chronic form in which the lesions are made up of endothelial cells with no giant cells nor other hall mark of the disease. These cases present a certain difficulty in diagnosis unless one is aware of their existence.

For the first few days the tubercle consists entirely of the phagocytic endothelial cells and giant cells, although in cases where a very large dose has been used the irritation may be so great as to cause the temporary outpouring of a flood of polymorphonuclear leucocytes. By the end of a week *lymphocytes* begin to make an appearance, small dark cells with a darkly staining nucleus and scanty cytoplasm, identical in structure with the lymphocytes of the blood, but probably derived

from the cells of the perivascular lymphatic sheath or other lymphoid tissue. They probably perform some important protective function, for Murphy has shown that if the lymphoid tissue of an animal is damaged by X-rays the disease will progress much more rapidly. At this stage the tubercle presents, in hematoxylin and eosin preparations, a dark blue peripheral ring of lymphocytes surrounding a central pink mass composed of endothelial cells with their pale nuclei, and an occasional giant cell, intermingled with which are a few blue lymphocytes.

The tubercle is non-vascular. The reaction is a cellular proliferation, and does not include the formation of any new blood vessels.

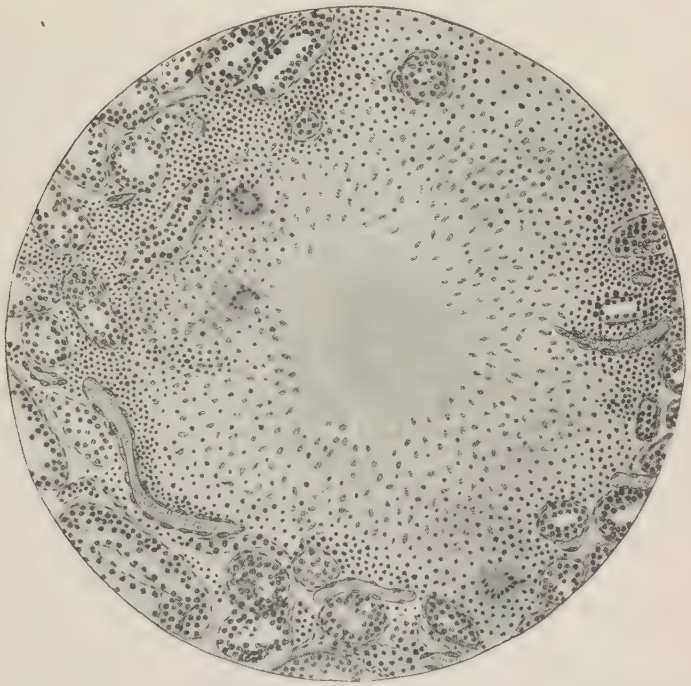

FIG. 15.—Tuberculosis of the testicle. The center of the affected area is completely caseous, further out are endothelial cells, whilst on the outskirts are giant cells and lymphocytes.

This non-vascularity has an important influence on the production of caseation.

By the end of the second week *caseation* has begun to appear in the center of the tubercle follicle. The cells in the center lose their outline and structure, undergo necrosis, and appear to fuse together, so that a granular structureless material is formed, staining diffusely with eosin, dry and cheesy in consistence. This coagulation necrosis is due partly to lack of blood supply, partly to the action of the bacterial toxins. The tubercle bacillus produces no exotoxin, but on disintegrat-

ing it liberates a slowly acting endotoxin which causes necrosis of the surrounding tissue. This disintegration is effected by the action of the cells which make up the tubercle follicle.

Reference has already been made to the fact that the type of reaction to an injection of tubercle bacilli depends largely upon whether the animal is tubercle-free or already suffers from tuberculosis. In the former case it is essentially sluggish and is proliferative rather than inflammatory. In the latter the response is rapid and is essentially inflammatory and exudative; there is an outpouring of leucocytes and of serum. The reason is that the animal is in a state of allergy, and the chief manifestation of the allergic state is this immediate inflammatory response. The difference in the two reactions is beautifully shown by skin inoculation tests, and this forms the basis of the well-known von Pirquet cutaneous reaction.

In the course of two or three days the inflammation subsides and is succeeded by the slow cellular proliferation which results in the formation of a tubercle. It will be obvious that this must be the course of events in the spread of human tuberculosis throughout the body, for once the initial lesion has become established the patient is in a constant condition of allergy.

One of the most important differences between primary infection and reinfection, as seen in the tissues of the guinea pig, is that there is a much greater tendency to breaking down in the latter lesion than in the former. This was first described by Robert Koch in 1891, and is known as the *phenomenon of Koch*. Its true significance, however, was not recognized for many years till it was demonstrated by Calmette and other workers. The object of this manifestation of allergy is to rid the body of the invading microörganisms. It is a defense reaction. If the tuberculous tissue breaks down and is discharged on the surface large numbers of bacilli are expelled from the body. As Calmette says: "For every bacillary reinfection the already tuberculous organism reacts in a more intense and rapid manner to expel the invader; it becomes more and more intolerant of the bacillus. The latter constitutes for the cells a more and more violent poison. This intolerance and this increasing hypersensitiveness manifest themselves by a tendency to more rapid caseation, to purulent softening of the tubercles, and to prompt expulsion of their contents." This protective reaction, however, may be carried to extremes, just as in the case of inflammation, the tuberculous organ may become progressively destroyed, and the phthisical patent may succumb despite or rather by reason of the immunity which he has acquired.

The Future History of the Tubercle.—The future history of the tubercle varies greatly depending on whether the forces of destruction or conservation prove the more powerful. The sequence of events may be one of the following:—

1. New tubercles may be formed in the adjoining tissue, which coalesce with the original tubercle till large areas of caseation are produced. These areas are usually very irregular in outline, but in the

brain and more rarely in the liver large spherical "solitary tubercles" may be formed.

2. The irritation produced may be so great, owing to the presence of excessive numbers of bacilli, that a typical acute inflammatory reaction is the result, with abundant migration of leucocytes and exudation of serum, obscuring to a large extent the tuberculous nature of the infection. Such a course of events is well seen in tuberculous meningitis and acute pneumonic phthisis.

FIG. 16.—Tuberculous cervical lymphatic glands. The glands are largely occupied by yellow, opaque, homogeneous areas of caseation.

3. In some cases there is an intermediate condition with the production of a granulation tissue without caseation, identical with that of ordinary inflammation save for the presence of numerous tubercles. This may be seen in the synovial membrane of joints, in the hyperplastic form of tuberculosis which occurs at the ileo-cecal junction, and in other positions.

4. Finally, the reaction on the part of the tissues may be sufficient to limit the spread. The fibroblasts proliferate, forming a fibrous zone around the tuberculous area walling it in, so that the caseous area becomes enclosed in a fibrous capsule. In such an area bacilli

may remain viable for long periods, but in a quiescent condition, so that the patient shows no symptoms of the disease. Or the fibrous tissue may invade the follicle, converting it into a fibrous mass, in which lime salts may be deposited in considerable amount, the result being a so-called *healed tubercle*. This last change is fortunately of common occurrence, as the calcareous masses so frequently found in the lungs and mediastinal glands testify. Even in the healed tubercle, however, living tubercle bacilli can usually be demonstrated by animal inoculation.

Method of Spread.—There are four chief methods by which the infection may spread.

1. By permeation.
2. By the natural passages.
3. By the lymph stream.
4. By the blood stream.

1. *By Permeation.*—Owing to the movement of the endothelial cells the bacilli are carried beyond the limits of the original tubercle and thus the disease spreads. It creeps along the tissue and lymph spaces, and owing to the irregularity of these spaces the resulting tuberculous area is correspondingly irregular. In such an organ as the brain where there are equal facilities for spread in every direction, a tuberculous tumor-like mass as large as a tangerine orange may be formed, the "solitary tubercle" or tuberculoma. In the liver, although more rarely, the same formation may occur.

2. *By the Natural Passages.*—Tuberculosis shows a great tendency to creep along a tube, a tendency never seen in syphilis. It may spread from the kidney down the ureter to the bladder, from the testicle up along the vas deferens to the bladder, or up one bronchus and down another.

3. *By the Lymph Stream.*—Tuberculosis, like syphilis may be regarded as primarily a disease of the lymphatic system. Unlike syphilis the lymphatic glands often offer a successful resistance to the spread of the disease, but equally often the barrier is broken down, and the infection spreads along the lymphatic vessels. The bacilli may be carried by the lymph stream into the circulating blood.

4. *By the Blood Stream.*—The blood is infected by way of the lymphatics, or occasionally by the tuberculous process involving the wall of a blood vessel, with the formation of miliary tubercles within the wall. From these foci bacilli are sown broadcast throughout the body, giving rise to *general miliary tuberculosis*, a condition in which the rapid growth and breaking down of the bacilli results in a severe toxemia accompanied by fever, and usually terminating in death in the course of a few weeks. Tubercles, often hardly visible to the naked eye, are found in almost every organ in the body, and the end is often due to tuberculous meningitis. The number of tubercles scattered throughout the body is so immense that it is hardly possible that they can all be due to the discharge of bacilli from one ulcerating

tubercle. It is more probable that secondary tubercles are formed in the vessels, and that from these the infection is once again poured into the blood stream.

Tuberculous Pus.—Typical caseous material is dry, granular, and cheese-like. It is high in unsaturated fatty acids which inhibit the action of proteolytic ferments. When these acids become saturated, either through the administration of iodides or as the result of a natural process, the ferments have free play, and may produce rapid softening and liquefaction of the caseous material. The result is the formation of a thick creamy fluid, to which the name of tuberculous pus is given, and the condition is called a *cold abscess*. The fluid is not true pus, but consists mainly of fatty débris floating in a serous fluid, intermingled with which are a few necrotic cells. It is usually sterile.

A *cold abscess* is so named because it is a soft, fluid swelling without the signs of acute inflammation. It is slow and insidious in onset and may be mistaken for a cyst, a gumma or a fatty tumor. The wall of the abscess is lined by granular, caseous material, which may contain tubercle bacilli. The outer layers consist of granulation tissue in which caseation has not yet occurred.

Opening and drainage of a tuberculous abscess, even under the most aseptic of conditions, is almost certain to be followed by invasion by pyogenic organisms. The condition is then said to be one of *mixed infection*, and the last state of that man is much worse than the first, for such constitutional symptoms as hectic temperature, wasting, and night sweats appear and dominate the picture. For this reason drainage of a tuberculous abscess is almost invariably bad practice.

Tuberculin is of considerable importance in the diagnosis of tuberculosis, and of some value in the treatment of surgical forms of the disease. It has been considered in the chapter on Surgical Bacteriology.

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CHAPTER VII

SYPHILIS

Syphilis is an infectious disease caused by the Spirochæta pallida, which enters through the skin or mucous membrane, producing a local lesion, and is then disseminated by the blood stream throughout the body. The disease occurs in two forms, the congenital and the acquired.

The Spirochæta Pallida.—The spirochæta pallida, discovered by Schaudinn and Hoffmann in 1905, is a delicate spiral-shaped organism, actively motile, 7 to 14μ in length (from once to twice the diameter of a red blood corpuscle) and 0.1 to 0.2μ in thickness. The epithet pallida is earned by the pale appearance of the organism in stained smears.

It is present in all syphilitic lesions, although much more readily demonstrated in primary and secondary lesions than in those of the tertiary period. Any lesion, therefore, of whatever date, from the surface of which there is a discharge, must be regarded as potentially infectious. During the earlier stages the organisms are found in the circulating blood. The most dangerous lesions are the primary sore and such superficial lesions of the skin and mucous membranes in the florid secondary stage as condylomata and mucous patches.

There are three methods by which the spirochete may be demonstrated.

1. *By Dark-ground Illumination.*—The discharge from the sore is examined by the dark-ground method, the active to-and-fro movements of the spirochete rendering its detection comparatively simple. When the apparatus is available this is the best method for early diagnosis.

2. *By Stained Smears.*—For this purpose Giemsa's stain or Leishman's stain will be found the most convenient. The spirochete is stained a faint pink. Or a drop of the secretion may be mixed with a drop of Indian-ink (Chin-Chin), and a smear made, the spirochete standing out unstained against the black background. The Congo-red method is similar in principle, a smear made with a 2 per cent solution of Congo red being then treated with sulphuric acid.

3. *By the Levaditi Method.*—Spirochetes in the tissues can only be demonstrated by the silver impregnation method of Levaditi, which stains the spirochetes black. The method on account of its technical difficulty is only of value in the hands of an expert.

In using the first two methods care must be taken not to confuse the sp. pallida with the sp. refringens, an organism often found on skin surfaces. It displays more numerous and more abrupt spirals than the sp. refringens.

The spirochete is a delicate organism which is readily killed outside the body by drying and by weak antiseptics. It is grown in culture only with great difficulty. It is strictly anerobic, and is best cultivated on serum agar containing a small piece of sterile tissue.

The disease can be transmitted experimentally to animals, not only to the higher apes, but to the lower monkeys and even to rabbits. It is only when the virus is inoculated at certain sites that the disease will develop with certainty: the genital organs in the monkey, the scrotum and testicle in the rabbit. Elsewhere the spirochete fails

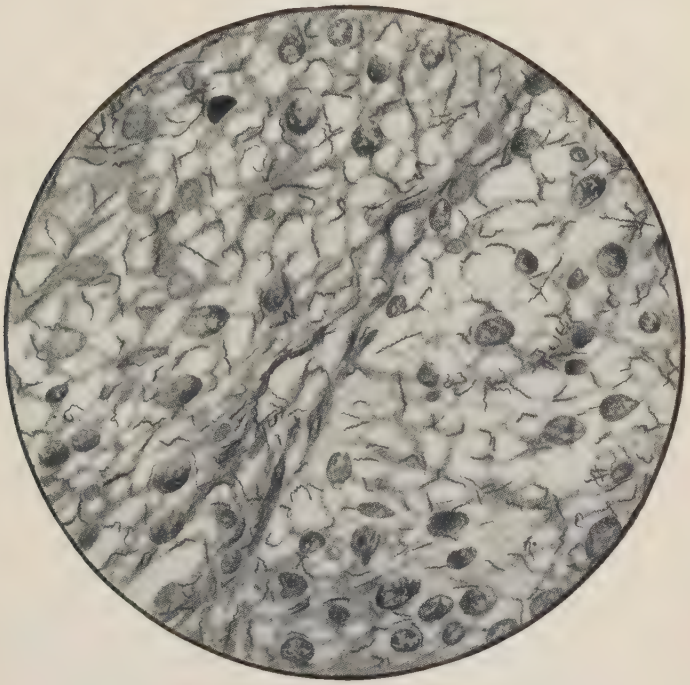

FIG. 17.—Spirochæta pallida in primary syphilitic lesion.

to gain a hold. The work of Brown and Pearce on the rabbit is especially worthy of note.

This is not the place in which to discuss the unorthodox views held and ably championed by McDonagh, but they cannot be allowed to pass unnoticed. McDonagh claims to have shown that the spirochæta pallida is the adult male form of a protozoal organism which he calls the leucocytozoon syphilidis, that the female form can also be demonstrated in microscopic preparations, that neither of these represents the infective stage, and that the parasite passes through a definite life cycle. In McDonagh's own words: "I believe that the spirochæta pallida is only the adult male form of a coccidial protozoon; that the complement fixation test is merely a physical reaction depen-

dant upon the increased number and size of the protean colloidal particles in the serum; and that salvarsan only destroys the parasite indirectly by increasing the oxidizing action of the host's protective substances."

For clinical purposes the disease is usually divided into three stages, primary, secondary, and tertiary, but the essential pathology in every stage is the same. Whether it be a primary chancre, a skin lesion, a mucous patch, an aortitis, a gumma, or a brain lesion in general paresis, the nature of the process is uniform, varied only by accidents of time and opportunity.

The several stages are separated by curious intervals of latency, during which the patient may experience no symptoms. During these periods, however, the spirochetes are by no means latent. It is the distinction, which we have already observed in tuberculosis, between infection and disease. The latent period does not indicate that the organisms are spreading to distant and hitherto unifected organs, for it has already reached them by the blood stream. It signifies rather that the tissues are undergoing a vital change, are developing a hypersensitiveness, on account of which they will react to the irritant with the production of the symptoms of disease. The organs differ in the time they take to develop this hypersensitiveness, the skin early, the central nervous system late, so that disease appears at different periods, but infection is there from a very early date. It is significant to note that Brown and Pearce in their experimental work on the rabbit have shown that although the defensive reaction may succeed in neutralizing the power of the spirochetes to produce disease, the infection is never abolished.

The same workers have formulated what they call the law of inverse proportions. The duration of a lesion, that is to say an active manifestation of the disease is inversely proportional to the intensity and extent of the local reaction. The same is true for the disease as a whole, so that severe early lesions are likely to be associated with mild manifestations in the later stages, whereas disastrous late results may have been preceded by early lesions so slight as to have escaped the notice of the patient, a fact which considerably increases the difficulties of diagnosis.

The different stages recognized by the clinician represent varying stages of reaction rather than varying stages of infection. Indeed the spirochetes are disseminated throughout the body and a condition of syphilitic septicemia set up at an extraordinarily early date. In patients who have died from accident when the primary sore was still fresh the infection was found to have spread through the lymphatic vessels and the lymph glands and to have reached the thoracic duct, so that blood infection had almost certainly occurred in this the first stage of the disease. Neisser was able to demonstrate spirochetes in the central nervous system of apes 10 days after inoculation, even before a local sore had fully developed. As Clifford Allbutt remarks: "From the first the seed spreads secretly; and when the circulatory

system is clotted up by the parasite the time for effectual intervention is past. 'Take these foxes while they are little.' "

Infection in the great majority of cases is acquired during sexual intercourse. It may occur, however, in other sites than the genital organs. Of these the most important are the lips, the fingers, and the nipple. The spirochetes usually enter through some crack or abrasion, but they may penetrate an uninjured mucous membrane.

Following the infection there is a latent period, usually of 3 or 4 weeks, but this may be as short as 2 or as long as 6. Long before this period has elapsed the blood stream is invaded, and systemic infection occurs, a syphilitic septicemia. At the end of the first latent period the primary lesion makes its appearance.

A second latent period now supervenes during which, although the spirochetes have been disseminated throughout the body, there is no sign of their presence. At the end of from 2 to 3 months after infection the tissues of ectodermal origin have apparently acquired the power to react, and lesions appear in the skin, mucous membranes, and central nervous system. These lesions may persist for 6 to 12 months or more, leaving no trace except perhaps for some pigmentation of the skin.

Again the patient may have an intermission during which he thinks that all is well, but tissue changes in the internal organs are going on, slowly but remorselessly, and one, two, or it may be many years later, these begin to tell their tale.

Pathological Histology.—The clinical manifestations of syphilis are protean and complex, but the pathological histology is constant and simple. The syphilitic lesion consists of a mass of granulation tissue; it is a granuloma. In the primary and secondary lesions this tissue is vascular and highly cellular, and the condition may terminate in resolution. In the later or so-called tertiary lesions the new cells become converted into fibrous tissue, the vessels obliterated, with a resulting degeneration of the parenchymatous cells, so that there is either a diffuse scarring with atrophy of the parenchyma, or the formation of caseous masses called gummata. The early lesions occur in vascular, the later in relatively non-vascular organs.

It has been said that syphilis loves the blood vessels, and it is indeed *par excellence* a vascular disease. But it is even more a disease of the lymphatic system. It is by the lymph vessels that the spirochetes first spread from the initial lesion, and it is through the lymphatics that the blood vessels are infected. Perhaps the most characteristic single feature is the perivascular infiltration of round cells which surround the smaller vessels as with a collar. These cells are contained in the perivascular lymph spaces. The round cell infiltration so characteristic of syphilis of the aorta commences in the adventitia, and in that part of the aorta (the arch) with the most abundant lymphatic supply. The endarteritis seen in the small vessels is not an exclusive sign of syphilis; it is found in tuberculosis and other chronic infections.

Immunity.—Syphilis, like several other infectious diseases, conveys a marked degree of immunity. It is a mistake to think, however, that this can never be overcome. Many undoubted cases have been recorded in which a patient suffering from active syphilis acquired a second infection.

Nor is it any longer possible to uphold the time-honored Colles' law, which states that a healthy woman bearing a syphilitic child will not

FIG. 18.—Syphilitic aortitis; perivascular infiltration in the media, thickening of the intima.

acquire the disease. The mother will not acquire syphilis, it is true, but she is not healthy, for she already harbors the spirochete, as is shown by the fact that her blood will give a positive Wassermann reaction.

A brief summary of the varied lesions of syphilis may now be given, but the conditions of special surgical importance will be considered in greater detail in later sections.

THE PRIMARY LESION

The *primary lesion* or chancre commences as a nodule, not as a sore. In most cases, however, the surface becomes abraded, so that an ulcer

is produced, the chief characteristic of which is the marked induration both of the floor and edges, which earns for it the epithet "hard." It is of great importance to note that this induration does not appear for several days, else the correct diagnosis may be missed in the earliest stage. The induration is due to the cellular infiltration and formation of new tissue which is the essential pathological lesion in syphilis. It may be so marked as to give the chancre a feeling as of a button of

FIG. 19.—Chancre of the tongue, two weeks old. (Edward Martin in Keen's Surgery.)

cartilage when pinched between the finger and thumb. The floor of the ulcer is dull red, later becoming coppery and glazed, or it may be covered with a grey false membrane. The discharge is thin and watery, and contains the spirochæta pallida in large numbers. There is no pain, and the chancre is insensitive. The lesion heals in the course of a few weeks, and leaves no scar if there has been no destruction of tissues.

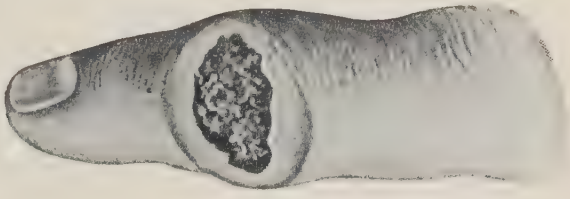

FIG. 20.—Chancre of the finger, two weeks old. (Edward Martin in Keen's Surgery.)

In congenital syphilis the primary lesion is in the placenta. There is therefore no primary stage in the child.

The **microscopic appearance** is that found in the early stage of all syphilitic lesions, but is lacking in distinctive features, and is much less readily recognized than the lesions of tuberculosis. Syphilis is mainly a disease of the blood vessels, and even at this early stage this characteristic is in evidence. There is a great formation of new

vessels, and about these there is a perivascular accumulation of lymphocytes, plasma cells, and endothelial cells. Large pale cells of irregular outline with vesicular nuclei may be seen. These are pro-

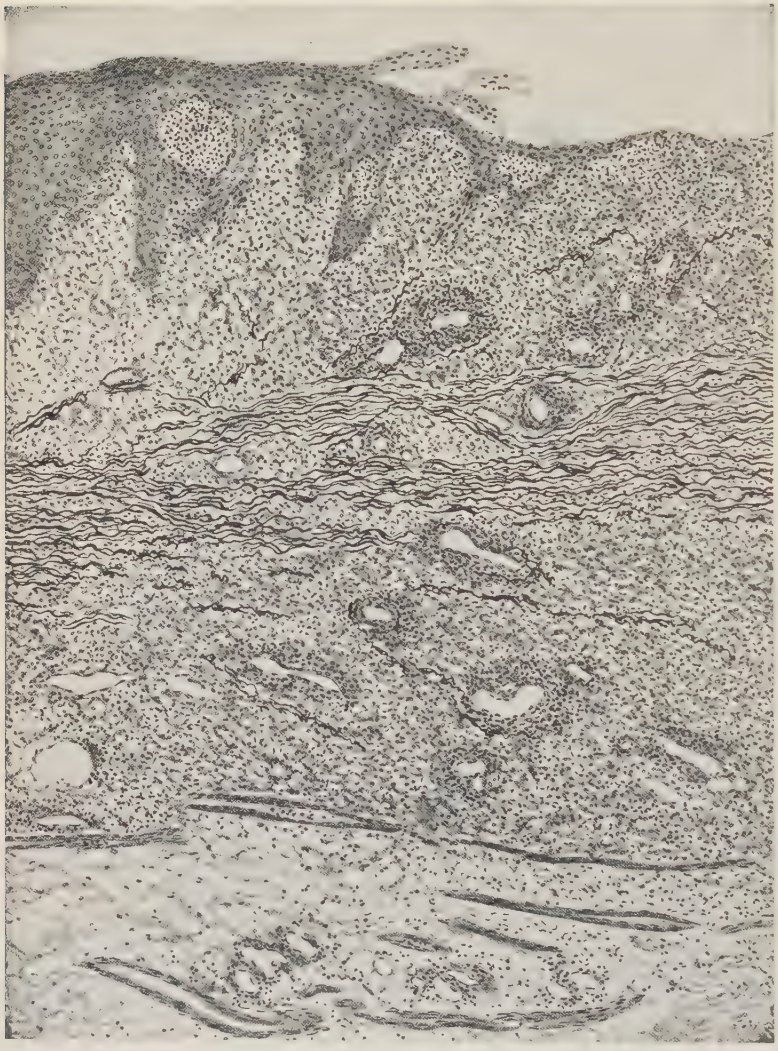

FIG. 21.—Edge of chancre, showing ulceration through the epidermis and great accumulation of mononuclear cells, especially about the vessels and lymphatics. (MacCallum.)

liferating fibroblasts, which may later be responsible for the formation of scar tissue. The inner coat of the arteries may be thickened even

thus early, a condition of endarteritis obliterans. There is stasis of the vessels from pressure of the accumulated cells, causing hemorrhage with the liberation of blood pigment which is responsible for the coppery pigmentation so characteristic of syphilitic lesions. The sp. pallida may be demonstrated by means of the Levaditi method.

Chancre and Chancroid.—The condition with which a chancre is most likely to be confused is chancroid or soft sore, an acute inflammatory lesion produced by Ducrey's bacillus, and acquired through sexual intercourse. The important points of distinction are as follows:

	Chancre	Chancroid
1. Incubation period	2–4 weeks.	2–4 days.
2. Number	Single.	Usually multiple.
3. Type of lesion	Proliferative.	Destructive.
4. Induration	Marked.	None.
5. Discharge	Thin and serous.	Purulent.
6. Spirochæta pallida	Present.	Absent.
7. Lymphatic glands	Not inflamed.	Inflamed, tender, suppurating.
8. Wassermann reaction	Positive after three weeks.	Negative.

It is of course possible to have a mixed infection, in which a chancre is superadded to a soft sore. In such cases the only certain method of diagnosis is the demonstration of the spirochete. It is therefore advisable to examine every case of soft sore for the spirochæta pallida, as the latter may be present in the sore for some weeks before the changes characteristic of a chancre make their appearance.

Primary Lymphatic Gland Enlargement.—At the end of the first or second week after the appearance of the chancre the lymphatics leading from it may be felt as thickened cords, and the glands in the groin on both sides become enlarged. They do not attain a size larger than a marble, are hard and shotty, discrete, and are not painful or tender. The condition ends in resolution, and the glands return to their normal size.

THE SECONDARY LESIONS

The secondary lesions are found mainly in the skin and mucous membranes, but the nervous system, the eye, and the bones and joints may all be affected.

At the end of the second latent period the patient commences to show signs of *constitutional disturbance.* There may be a varying degree of *fever.* The blood shows an *anemia,* often marked, and there may be an increase in the lymphocytes. *Cachexia* is of frequent

occurrence, the patient developing a pale, sallow complexion, and showing perhaps some slight wasting.

Lymphadenitis is one of the earliest and most constant features of this stage. The glands throughout the body become enlarged and indurated, there is an absence of inflammatory changes, and the enlargement persists for several months and sometimes years. Enlargement of the epitrochlear and posterior cervical glands is of special diagnostic value. Resolution ultimately occurs.

The skin is the seat of lesions bewildering in their number and variety and simulating many other skin diseases, but displaying certain common characteristics. They are symmetrical in distribution, polymorphous in type, so that several varieties may be present at the same time, thus differing from ordinary skin rashes, present an outline corresponding to a segment or the whole of a circle, possess a coppery tinge, heal as a rule without destruction of tissue, and respond readily to treatment. The particular lesion depends on the degree of the inflammatory process. The *macular* rash, resembling that of measles, results where the vascular changes are marked with but slight cellular infiltration. When there is an abundant collection of cells the lesion becomes *papular*. In the later stages it may become *pustular*, and rounded necrotic patches covered by a crust are formed, the condition termed *rupia*. Another late manifestation is a scaly eruption of the palms of the hands and the soles of the feet, a condition extremely suggestive of syphilis.

A common form of lesion of the skin is the *condyloma*. This is a flat elevation, moist, loaded with spirochetes, and extremely infectious. Condylomata occur where two skin surfaces are in contact and consequently moist, as in the anal folds, the vulva, and between the thighs.

The hair and nails are often affected, owing to the inflammation extending down into these appendages of the skin. The hairs fall out, giving rise to a partial alopecia, patches on the back of the head losing some but not all of the hair and having a "moth eaten" or "mangy" appearance. The nails become dry, brittle, and fissured, a condition of onychia.

Mucous Membranes.—In the mouth and pharynx *mucous patches* are of very common occurrence. They are flat raised patches, milky in color, surrounded by a narrow red border, and often likened to the track of a snail. Frequently they become ulcerated, and discharge great numbers of spirochetes. They also occur in the vaginal mucosa. They are due to inflammatory proliferation of the surface epithelium.

The Central Nervous System.—Until recently it was considered that involvement of the central nervous system occurred only late in the disease. It is now known that it may be one of the earliest organs involved. Examination of the cerebrospinal fluid shows the changes characteristic of meningeal irritation, namely lymphocytosis and an increase in the globulin content. The neuralgic pains and ocular palsies of the secondary stage are dependant on the same cause.

The Eye.—Iritis is of common occurrence at this stage and differs in no way from that due to other causes. Retinitis may occur, but is more characteristic of the later stages.

Bones and Joints.—Periostitis is a common early sign, and may appear at the same time as the rash. Usually, however, it does not come on till a few months later. The bones commonly affected are the tibia, clavicle, sternum, and cranial bones. A painful, tender, elastic swelling forms over the bone. The pain is usually worse at night, owing to the increased vascularity when the patient is warm in bed.

One or more joints may show a subacute inflammatory swelling with little pain or tenderness. The knee is most often affected. The condition terminates by resolution.

THE TERTIARY LESIONS

Although no hard and fast line can be drawn between secondary and tertiary syphilis, the secondary lesions sometimes appearing late and the tertiary early, yet there are important differences between the two varieties. The tertiary lesions are not symmetrical, they affect the deep organs as well as the superficial structures, they contain few spirochetes, and they show a tendency to destruction which is not seen in the earlier lesions.

Until very recently it was considered that the most important manifestation of tertiary syphilis was the localized degenerative lesion known as the gumma. The revolutionary researches of Scott Warthin have placed the matter in an entirely new light. He has shown that the gumma is of rare occurrence compared with a chronic mild inflammatory condition associated with diffuse infiltration of the parenchymatous tissues, and resulting in fibrosis. By dint of most painstaking and laborious search Warthin has been able to demonstrate that spirochetes are present in the great majority of such lesions, and he considers that the lesion is so characteristic that a diagnosis of syphilis can be made even in the absence of spirochetes. The gumma is merely a localized manifestation of this diffuse process.

The Diffuse Infiltration.—As the result of the spirochetes settling in the tissues a slow inflammatory process is set up, and the part becomes infiltrated with small round cells and plasms cells, with an accompanying proliferation of fibroblasts. There is a formation of new vessels, and the result is a cellular granulation tissue, analogous to the granulation tissue that is sometimes formed in tuberculosis. The inner coat of the arteries of the part becomes much thickened, with narrowing of the lumen. In course of time the new connective tissue cells become converted into fibrous tissue, the parenchyma cells atrophy, and extensive scarring follows. The researches of Warthin, using the Levaditi method, have shown that this is an extremely common occurrence, and he has been able to demonstrate this lesion in the heart, pancreas, liver, adrenals, and other organs in the great majority of syphilitic cases which he has examined at autopsy. It is probable

that these changes give rise to disturbance of function such as myocarditis, diabetes, and other conditions whose syphilitic nature has not hitherto been suspected. Thickening of the base of the tongue and of the testicle are of value in autopsy diagnosis.

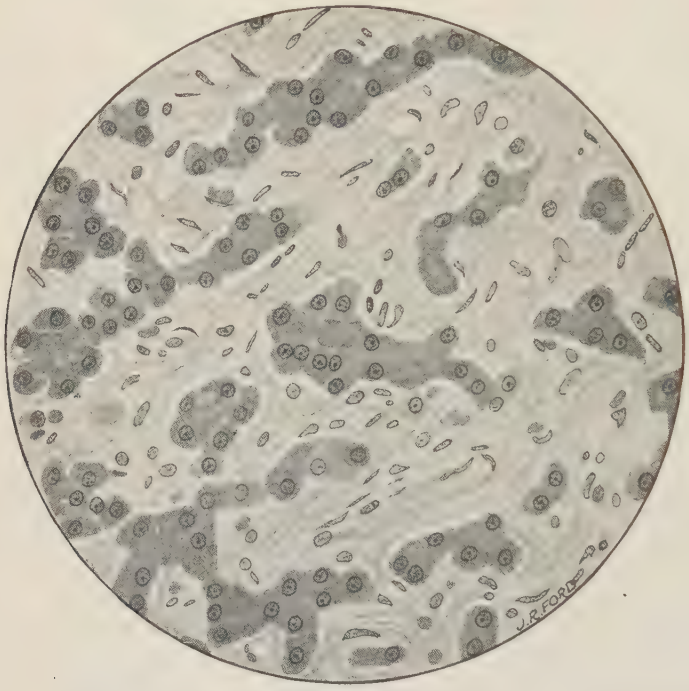

Fig. 22.—Congenital syphilis of the liver. A good example of the diffuse infiltrative form of the disease.

The Gumma.—The lesion may be localized, in which case a gumma is formed. The proliferating cells give rise to a definite nodule, the center of which undergoes caseation, due mainly to deficient blood supply from obliteration of the vessels. The caseation is seldom so complete as in tuberculosis, and traces of the original structure can usually be made out. Surrounding the caseous center are the usual lymphocytes and plasma cells, and further out there is a zone of proliferating fibroblasts or definite fibrous tissue. Giant cells similar to those of tuberculosis are of common occurrence, but are seldom so numerous as in the former disease. To the naked eye the gumma appears as a yellow homogeneous mass surrounded by fibrous tissue. When near the surface ulceration may occur.

The gumma when small may become invaded with connective tissue and fibrosed. As a rule, however, the caseous center remains unaltered. It does not liquify, because the proteolytic ferment necessary for such liquefaction is neutralized by the large amount of unsaturated fatty acid present, which acts as an antiferment by virtue

of its unsaturated state. When saturation is produced by means of potassium iodide, the proteolytic ferment quickly asserts itself, and liquefaction and absorption are the result.

Although from the medical standpoint the diffuse inflammatory lesion is the more important, from the surgical the gumma claims first place, and it will therefore be considered here.

Any organ of the body may be affected, but the common sites are the skin, the mucous membranes, the viscera, the bones, and the nervous system.

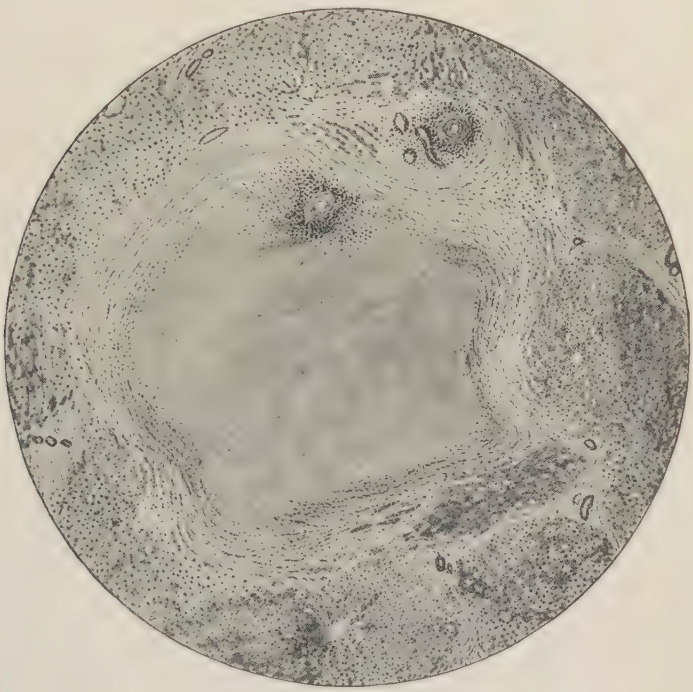

Fig. 23.—Gumma of the liver.

1. *The Skin.*—A gumma may commence in the skin, in which case it usually ulcerates early. Or it may be formed in the subcutaneous tissue, appearing as a hard, painless mass, freely movable, which disappears readily under treatment. It may also involve the skin and ulcerate. The characters of the syphilitic ulcer have already been described (page 63). Its punched-out character, serpiginous outline, and wash leather base are usually highly characteristic. It tends to heal at one point and break down at another, a method of spread responsible for the wavy character of the margin. When it heals it leaves a scar, at first pigmented, later becoming white. The knee is a favorite site for such scars.

2. *Mucous Membranes.*—*The tongue* may be the seat of a syphilitic glossitis. In the early stages the organ is swollen, red, moist and

painful. The papillæ disappear leaving the surface characteristically smooth, red, and glazed. Oval-shaped ulcers may form, which must be distinguished from those due to malignant disease. The latter occur at the edge of the tongue, whereas the syphilitic ulcer may occur on any part, but particularly in the center. It is not uncommon for carcinoma to develop on a tongue already damaged by syphilitic glossitis. As sclerosis occurs the tongue becomes indurated, and the smooth surface is broken up by numerous cracks and fissures.

The pharynx may be the seat of gummatous ulceration. Perforation of the soft palate may occur. The subsequent fibrosis may cause marked deformity.

The larynx is liable to similar changes. There may be ulceration, and later scarring, which greatly interferes with the action of the vocal cords, giving rise to a characteristic hoarseness of the voice.

The rectum is an important site for syphilitic disease, not because of its frequency, but on account of the liability to confusion with carcinoma. The wall of the rectum becomes thickened and ulcerated and later there may be a serious degree of stenosis. It is a condition which should always be considered before a diagnosis of cancer of the rectum is made.

The Viscera.—Gummata may occur in any of the viscera, but the liver is the most frequently involved. The gumma may heal with fibrosis, giving rise to deep radiating scars in the organ, so that the surface may become lobulated. Large gummata of the liver are seldom seen nowadays. Syphilis of the testicle is perhaps of the most interest to the surgeon. The organ may become the seat of a gumma, which may remain for years as a hard resistant mass, or may break down and ulcerate through the scrotum. Much commoner is a diffuse infiltration with fibrous tissue, causing a uniform enlargement of the organ. In both cases there is a characteristic loss of testicular sensation on palpation. The condition has to be distinguished from tuberculosis and carcinoma.

The Bones.—Either gummata or a diffuse periostitis may occur. The gumma forms an ill-defined mass, which is both tender and painful. It is usually absorbed, but may break down and ulcerate. The tibia and the cranial bones are common sites. The condition may be mistaken for sarcoma.

The Nervous System.—To the physician the subject of cerebrospinal syphilis is of the first importance, but to the surgeon the chief lesion of interest is the gumma, which may produce all the symptoms of a cerebral neoplasm. It usually grows from the meninges, but may occur in the substance of the brain. An examination of the cerebrospinal fluid will throw valuable light on the nature of the condition, as a moderate increase in the globulin and lymphocytes will be found. The Wassermann reaction is usually negative in the fluid. The findings are not nearly so marked as in general paresis and tabes dorsalis, conditions in which the parenchymatous tissue of the brain and cord is involved.

CONGENITAL SYPHILIS

Syphilis may be inherited from either the father or the mother. In all cases of paternal transmission the mother is also infected, although she may display no symptoms of the disease.

The child may be born dead, or alive with abundant evidence of syphilis, or apparently healthy, the lesions not appearing for several weeks.

Much the same organs are involved as in the acquired form, namely the skin and mucous membranes, the bones, the viscera, and the eye and ear. The lesions also are similar except that the diffuse inflammatory infiltration of parenchymatous organs is very much in evidence. The child shows no primary lesion, for that occurs in the placenta.

The *skin* is the seat of a variety of eruptions, varying from rose or copper-colored spots to vesicular or even pustular forms. The buttocks, the neighborhood of the anus, the angles of the mouth, and the palms of the hands and soles of the feet are favorite sites. Lesions in the last-named position are scaly in type with much desquamation. The lesions around the mouth leave pale radiating scars from which a diagnosis may be made in future years. The whole skin may be dry and wrinkled giving to the child a prematurely old and wizened appearance.

Mucous Membranes.—Inflammatory lesions similar to those of acquired syphilis are common. One of the earliest symptoms is due to inflammation and ulceration of the mucous membrane of the nose, giving rise to the difficulty in breathing known as "snuffles." The diarrhea frequently present is probably due to a similar condition in the intestine.

The Bones.—Two chief types of lesions are met with, the atrophic and the productive; the former are rare, the latter common.

In the *skull* there may be atrophy of the cranial bones at the points of greatest pressure with marked thinning, giving rise to the same condition of "craniotabes" as is found in rickets. The productive form is dependent on a syphilitic periostitis, affects the frontal and parietal bones close to the middle line in the region of the anterior fontanelle in a remarkably symmetrical manner, and gives rise to the formation of rounded bosses of bone, sometimes as much as half an inch in thickness, of highly characteristic appearance.

The *long bones* may be the site of productive changes giving rise to the formation of gummata and osteophytes, or there may be a fairly uniform thickening of part of the bone from periosteal activity, often altering the contour as in the sabre-shaped tibia. Atrophic lesions may occur at the epiphyseal ends of the bones, accompanied by absorption of the bone and separation of the epiphysis.

The teeth show characteristic changes. Not the milk but the permanent teeth. The typical teeth, known as "Hutchinson's teeth" after Sir Jonathan Hutchinson who was the first to describe them

accurately, are small and ill-developed, more widely spaced than normal, narrower at the apex than at the base so as to appear peg-shaped, and usually display a central notch. The teeth principally affected are the upper central incisors. Recently it has become recognized that the six-year molars are affected in congenital syphilis much more regularly than are the central incisors, and in even more characteristic fashion. The grinding surface is eroded, and the greater part of the surface of the molar becomes pitted, excavated, and discolored. The condition has been called the "honey-combed molar of hereditary syphilis."

The Eye.—About the age of puberty an interstitial keratitis often develops, affecting first one eye and then the other, and producing a ground-glass opacity, which usually clears up to a great extent, leaving only a few opaque patches.

The Ear.—Quite early in the disease a marked degree of deafness may develop, which is apparently central in origin. The middle ear may also be the seat of syphilitic inflammation.

A patient presenting interstitial keratitis or the resulting opacities, Hutchinson's teeth, deafness of central origin, and radiating scars at the angles of the mouth has all the hall-marks of congenital syphilis.

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CHAPTER VIII

SPECIAL WOUND INFECTIONS

ERYSIPELAS

Erysipelas is an acute inflammation of the lymphatics of the skin or a mucous membrane due to the entrance of the Streptococcus pyogenes through a wound. This wound may be so minute as to escape notice, but a break in the surface is always present.

At one time it was supposed that the condition was due to a special variety of streptococcus, the streptococcus erysipelatis, but it is now known to be caused by the ordinary hemolytic streptococci, although apparently modified by conditions which are not yet properly understood. In rare cases other pyogenic bacteria may be the causal factor, such, for instance, as the staphylococcus, the colon bacillus, etc.

In 90 per cent of cases the face or scalp is the site of the inflammation. It is probable that in very many of these cases the starting point is a latent infection of the nose or nasal sinuses. It may follow operations which lay open a diseased middle ear or mastoid cells. In the remaining cases the leg or foot is generally affected. In the newly-born the umbilical cord may be infected. The mucous membrane of the mouth or of the vagina may occasionally be involved. The relation of erysipelas to puerperal fever is well recognized.

Some persons are liable to recurring attacks of erysipelas, showing that the factor of the patient is of importance as well as the factor of the bacteria. On the other hand it not infrequently happens that an attack of erysipelas is followed by the improvement or recovery of a morbid condition from which the patient may have suffered for a long time. Such conditions are chronic eczema, old ulcers of the leg, and even innocent and malignant tumors. It is on this fact that the use of Coley's fluid, which contains the toxins of the streptococci of erysipelas, is based. I have even seen a case of chronic melancholia recover as the result of a sharp attack of erysipelas.

Erysipelas used to be regarded as an extremely infectious condition. The infectivity, however, depends entirely on the presence of a discharge containing the causal bacteria. If the skin is unbroken there is no danger of infection.

Morbid Anatomy.—The disease spreads from the site of inoculation as a drop of grease spreads on a piece of paper. The advancing margin is of a bright or dull red color, and slightly raised above the general surface. The margin itself is irregular in outline, and has been aptly likened to the burnt edge of a smouldering sheet of paper. Just beyond the sharp margin the lymphatics are crowded with streptococci.

The margin itself shows acute congestion and the lymph spaces of the corium are crowded with cells. The inflammatory cells are mainly lymphocytes and wandering mononuclear cells. It is certainly remarkable that whereas in ordinary streptococcal infections the characteristic defense cell is the polymorphonuclear leucocyte, in erysipelas the cellular exudate should be mainly composed of small mononuclears. The center of the patch may show astonishingly little change. Indeed in the milder cases it is as if a wind had swept over a cornfield, producing a well-marked temporary wave, but leaving no permanent trace to tell the tale. There is a notable absence of pus formation.

Such is the typical form of erysipelas, involving essentially the epidermis. In more severe cases the deeper tissues may be involved, thrombosis may occur with tissue death, suppuration is marked, and the superficial layers of the epidermis are raised into blebs containing serum, or into pustules filled with pus. These deeper forms are true examples of cellulitis. In some cases the inflammatory exudate is rich in fibrin, with the result that the affected part manifests a brawny induration.

General symptoms of intoxication such as high fever and a well marked leucocytosis are present in the great majority of cases. In rare instances there may be a complete absence of fever. The constitutional symptoms are not due to an invasion of the blood stream by the streptococci, but to the absorption of the toxins produced locally. Occasionally a general septicemia may occur, being usually attended by a fatal result.

The only treatment for erysipelas which can hope for success must be directed against the infecting streptococci. Many attempts at specific treatment have been made, but they have met with the same failure which has attended such efforts against other forms of streptococcal infection. Antistreptococcal serum has no more effect than water. The successful results attributed to it are due to the self-limited nature of the disease. There is little more to be said for the use of a stock streptococcal vaccine. It is extremely doubtful if it is of the slightest benefit.

TETANUS

Tetanus is an infective disease characterized by tonic and clonic spasms, and caused by the Bacillus tetani.

The tetanus bacillus lives in soil which has been manured. It is a normal inhabitant of the intestine of the horse and other animals. It occurs in the feces of grooms with great frequency and occasionally it may be found in the feces of ordinary individuals. Tenbreck and Bauer found it in 35 per cent of stools from 78 persons in Peking. Although, therefore, in the vast majority of cases tetanus is an infection of skin wounds, it may occasionally gain access to the tissues through an operation wound involving the bowel. It is true that in some of these cases of post-operative tetanus the infection has been due to

contaminated cat-gut or dressings. It is a mistake, however, to think that all cases can be traced to this source.

Pathology of Absorption.—In tetanus, as in diphtheria, the bacilli remain at the site of infection, whilst the toxins are absorbed and produce the general symptoms. The routes of absorption, however, are very different. In diphtheria the toxin is absorbed into the blood; in tetanus the toxin is absorbed by the motor end-plates, and passes to the spinal cord or the brain. This is the invariable route. Even when the toxin is injected into the blood stream it only produces its effects after it has been absorbed by the motor end-plates. No absorption occurs from sensory nerve endings.

The toxin ascends the nerves by way of the axis cylinders and by way of the lymphatic channels in the epineurium and perineurium. Although the toxin can only travel from the wound to the spinal cord via the motor nerves of the part, it may also pass along innumerable other motor nerves, for it is carried by the blood stream to all parts of the body, and is readily absorbed by any motor end-plate with which it may be brought into contact. It is this secondary mechanism which is responsible for the development of general as opposed to local tetanus, and it is by interfering with this mechanism that the prophylactic use of antitoxins is so efficacious.

It may be asked why it is that the first symptoms of tetanus appear in the muscles of the jaw and neck, and not in those of the affected part. The reason is that in man and other large animals it takes a considerable time for the toxin to travel up the long nerves from the hand or foot where the infected wound is usually located. The toxin is absorbed directly into the blood stream, reaches the motor end-plates throughout the body, and commences to travel up along the corresponding nerves. The nerves to the muscles of the face, the neck, and the back are so much shorter than the others that the toxin reaches the motor cells of these nerves before it has time to affect those of the limbs. In experimental tetanus in small laboratory animals, on the other hand, the toxins have a shorter distance to travel, so that the symptoms begin in the inoculated extremity, and death may occur before trismus or head retraction develop.

On reaching the cord the toxin becomes anchored to the motor ganglion cells. It also spreads to neighboring motor areas and to the sensory side of the cord. The fact that the toxin is so firmly anchored to the cells of the cord that it can not be dislodged by antitoxin has long been used as an argument against the therapeutic value of antitoxin, but, as Ashhurst has emphasized, if it can be shown clinically that antitoxin treatment is of undoubted value even after the development of symptoms, then the failure of the laboratory to explain that success may well be disregarded. Moreover, the antitoxin will neutralize the fresh supplies of toxin which are being constantly absorbed from the wound.

The **autopsy findings** are largely negative. Apart from some degeneration of the ganglion cells in the cord, and some congestion of

the grey matter of the pons and medulla, there is nothing to be seen to correspond to the terrible clinical condition of the patient. The alterations are of a molecular rather than a gross nature.

The **incubation period** is very variable, depending partly on whether prophylactic treatment has been employed, partly on the position of the wound. An average period is from ten days to a fortnight. When the seat of infection is on the face, the symptoms may appear in three or four days, as the toxin has a comparatively short distance to travel before it reaches the central nervous system. It may be stated as a general rule that the shorter the incubation period, the more severe is the attack and the higher the mortality. Occasionally months may elapse before the onset of the symptoms. In such cases the spores remain in the tissues in a quiescent condition, and are only aroused to activity by subsequent operative interference or merely by manipulation. This is particularly liable to occur in the case of operations for the removal of a foreign body, or in cases with dense scarring which facilitates the protection and encapsulation of the tetanus spores. This is a point of the greatest importance. In all cases where tetanic infection is suspected, a subsequent operation should be preceded by another prophylactic injection. This is made necessary by the fact that the antitoxin is all eliminated from the body in about 8 or 10 days. For this reason also it is wise to give a second prophylactic injection ten days after the original injury, and to repeat the injection as long as any necrotic material remains.

The characters of the tetanus bacillus are those of an anerobic, spore-bearing, Gram-positive bacillus. It is a slender rod with rounded ends. At incubation temperature it readily forms spores which give the organism a very characteristic appearance. They are several times the diameter of the bacillus, and as they are terminally situated they give it the appearance of a drumstick. The bacilli possess flagella, but are only feebly motile. In smears of pus from an infected wound some of the organisms may possess spores, but many may not, and appear merely as slender rods.

The tetanus bacillus will only grow under anerobic conditions, but may be cultured on ordinary media under these conditions. The task of separating it from accompanying organisms is facilitated by taking advantage of the heat-resisting property of its spores. A mixed culture is grown and is then heated to 80° C. for an hour. At this temperature the non-spore bearers are killed, and B. tetani can be obtained in pure culture.

The bacillus being a strict anerobe, its growth is greatly favored by the presence of other aerobic bacteria, so that it is never found in pure culture in a wound. Large, lacerated, infected wounds, plentifully contaminated with earth, are those which are liable to be the starting point of tetanus. Occasionally the break in the surface may be a mere scratch or pin-prick. It must be borne in mind that the presence of tetanus bacilli or spores in the tissues is not sufficient in itself to produce the disease. The bacilli were frequently found in

the wounds of soldiers who never developed any symptoms of tetanus. Tetanus is not merely a wound infection, but an infection of septic wounds.

In examining catgut for tetanus certain points must be kept in mind. The catgut used in surgical operations consists of the submucous layer of the small intestine of lambs. This is twisted tightly into strands, so that any tetanus bacilli which may be included are extremely well protected. Simple culture of such infected material may quite fail to demonstrate the presence of the bacilli. This can best be done by macerating the catgut or by implanting it in the tissues of a guinea-pig. By this means the imprisoned bacilli are liberated, and may be recognized either by their growth on artificial media or by their biological effect on the guinea-pig. It must be remembered that the necrotic material surrounding a piece of catgut in a case of post-operative tetanus may produce no effect when injected into an animal, but that the bacilli may be demonstrated in the catgut by the above-mentioned methods.

The **symptoms** of the disease need not be fully described here. They are due essentially to such a degree of sensitization of the motor apparatus that an extreme hypertonicity is produced, and the sensitive reflex arc reacts so readily that clonic spasms may result from the most trifling stimuli such as a breath of cold air, a light touch, the banging of a door, or even the act of swallowing. The whole motor system is in an explosive condition, and the explosions are terrible in their intensity.

Stiffness of the muscles of mastication, notably the masseters, producing a condition of "lock-jaw" is first noticed by the patient. The muscles of the neck, particularly the sternomastoid and trapezius, then share in the tonic contraction followed by the muscles of respiration, the diaphragm, and lastly the muscles of the limbs. Clonic spasms of increasing severity are superadded to the general condition of tonus. The patient may die in one of these spasms, or death may be due to asphyxia produced by the vice-like grip of the muscles of respiration.

Cephalic tetanus is a rare and interesting condition in which, as the result of a wound on the face, there develops a paralysis of the facial nerve on the same side together with a tonic contraction of the muscles supplied by the other cranial nerves, and, it may be, general tetanus. The facial paralysis is due to an ascending neuritis of the facial nerve with accompanying swelling and pressure on the nerve in the Fallopian canal.

Local tetanus was frequently seen during the war in men who had received a prophylactic injection of antitoxin. General tetanus failed to develop, but the muscles of the affected part became hypertonic, and in some instances clonic spasms appeared. The explanation of the condition is interesting. In an unprotected person the tetanus toxin, as already indicated, is carried throughout the body by the blood stream, so that absorption occurs along innumerable motor nerves in

addition to those of the part primarily involved. In the resulting general spasm the local condition is generally completely masked and attracts no attention. Although this general absorption is prevented by the use of antitoxin, the poison is still enabled to travel up the nerves from the wound, and this part alone subsequently shows the effect of the action of the toxin on the cord. A precisely similar condition is seen when tetanus toxin is injected into an insusceptible animal such as a cat. The part injected becomes hypertonic, but no general symptoms develop.

The *value of antitoxin treatment*, both prophylactic and curative, is considered on page 36.

ANTHRAX

Anthrax is an infectious disease common in herbivorous animals such as horses, cattle, and goats, and occasionally attacking man. Man may become infected in three ways: (1) through the skin (malignant pustule), (2) through the respiratory tract (woolsorters' disease), and (3) through the alimentary canal. The only form of interest to the surgeon is the wound infection which gives rise to malignant pustule.

Animals vary greatly in their sensibility to anthrax. Mice, rabbits, and guinea pigs are so susceptible that in them the disease is of a most fatal nature, practically invariably developing into a septicemia in which the blood and every organ in the body comes to swarm with anthrax bacilli. Enlargement of the spleen is so constant in susceptible animals that the disease is known as splenic fever. Pigeons, fowls, and rats, on the other hand, show a high degree of immunity, although that immunity may be broken down by adverse conditions. Man occupies an intermediate position, for in him the skin lesion may remain localized, or again a condition of general anthrax septicemia may develop. In the first case the prognosis is good, in the second it is usually regarded as hopeless.

The most important characteristic of the bacilli is their tendency to form spores outside of the body. The fact that no spores are formed within the body is of the greatest importance in indicating the means of disposal of the dead body of an animal suffering from the disease. If no blood is shed the ground in which the animal is buried soon becomes innocuous; if it is, the spores may lurk in the soil for many years, and form a constant menace to other animals.

The infection is conveyed from animals to man chiefly in infected wool or hides, so that the disease is commonest among wool-sorters, tanners, and others whose occupation lays them open to infection. A number of cases have been traced to the use of shaving-brushes made from infected material. I saw a most characteristic example of malignant pustule in France on the face of a soldier who had used his sheepskin coat as a pillow, and who had a slight abrasion on the cheek.

The disease commences as a small pimple, which rapidly develops into a vesicle, and is situated on an exposed part of the skin, usually the

face, neck, hands, or arms. The vesicle contains a clear serous fluid, never pus, so that the term malignant pustule is a misnomer. The vesicle bursts, and discharges a clear or blood-stained fluid, leaving a black slough. Around this black eschar a fresh row of vesicles is formed, and further out still there is a raised brawny induration. The bacteriological diagnosis is readily made by making smears of the fluid in the vesicles, which are found to be swarming with the characteristic large, thick, blunt-ended, Gram-positive bacilli.

At any stage the bacilli may enter the blood stream, giving rise to a fatal anthrax septicemia. The bacilli can then be demonstrated in blood culture.

The forbidding appearance of the anthrax pustule and its limited character has led to the adoption of excision as the popular method of treatment. This proceedure, however, may result in widespread blood dissemination. Much safer is the isolation of the pustule by a barrier of anti-anthrax serum injected subcutaneously, followed by a sterilizing dose of 150 to 200 c.c. of serum given intravenously. Even when a general septicemia has been demonstrated by blood culture, the intravenous use of large doses of serum may be followed by recovery.

FIG. 24.—Anthrax: malignant pustule. (Jacobi.)

GLANDERS

Glanders is a contagious disease of horses, from which it may be conveyed to man. It is therefore found in those whose work brings them in contact with sick horses: grooms, coachmen, veterinary surgeons, etc. Glanders may be regarded as one of the infective granulomata, and in its more chronic form is sometimes distinguished with great difficulty from tuberculosis, syphilis, or actinomycosis. When an atypical case of one of these diseases occurs in one closely associated with horses it is well to bear glanders in mind.

Quite recently I had an opportunity of studying a case of a chronic suppurative lesion of the muscles of the leg, which provided a difficult diagnostic problem. All the ordinary infective granulomata such as tuberculosis, syphilis, actinomycosis, blastomycosis, and sporotrichosis were considered and excluded. Then the patient happened to mention that he had been looking after two horses which had died of glanders. The pus was examined for glanders bacilli, and these were found (but not in direct smears) with the greatest of ease.

Bacteriology.—The disease is due to the Bacillus mallei. This is a slender Gram-negative organism rather similar to the tubercle bacillus. It is difficult to stain with the ordinary aniline dyes, and is best shown by means of weak carbol-fuchsin. For purposes of diagnosis the suspected material should be injected into the peritoneal cavity of a male guinea pig. In a remarkably short time, usually within 24 hours, a characteristic acute inflammation of the tunica vaginalis is set up. This is known as the Strauss reaction. The fluid from the tunica is inoculated on potato, where it produces a transparent growth which by the end of the third day has a yellowish honey-like appearance. The reaction on potato, together with the other characters already described, is pathognomonic of glanders.

Infection from the nasal discharge of a diseased horse occurs through a break in the skin of an exposed part such as the face or hand, or first involves the mucous membrane of the nose or mouth.

The **microscopic appearance** of the primary and also of the secondary lesions is in no way characteristic, being merely that of one of the infective granulomata, although without the distinguishing features of tuberculosis or syphilis. In the more acute lesions the picture may be that of ordinary suppuration. The specific micro-organism may be found in the discharge, although seldom in large numbers.

After an **incubation period** varying from a few days to two or three weeks a papule appears which soon develops into a pustule. A crop of pustules form which may be mistaken for anything from boils to small-pox. At a later stage the chief skin lesions may be large irregular ulcers discharging a foul blood-stained fluid. When the infection is in the nose the ulceration may involve the bones of the face.

The disease may run an acute or a chronic course. The *acute form*, which is invariably fatal both in horses and man, is characterized by a rapid spread of the surface infection, the formation of metastatic nodules and abscesses in the lungs, liver, spleen, and kidneys, and the development of the general symptoms of septicemia and pyemia.

In the *chronic form* the manifestations are protean, and the diagnosis often a matter of great difficulty. A nodular thickening of the lymphatics is very characteristic, especially in horses, and to this condition the term *farcy buds* is applied. Farcy is the name given to the chronic form as seen in the horse. The neighboring glands become swollen, and in addition to widespread ulceration there may be secondary deposits in the subcutaneous tissues and in the muscles. Indeed it may be said that glanders is a disease of lymphoid tissue, of connective tissue, and of muscle. In the only case which I have seen the destruction of the muscles of the leg was extreme, so that sinuses 6 or 8 inches in length were formed, but neither bones nor joints were involved.

The course of the disease may last for months or even for years. Anyone wishing to read a thrilling and dramatic description of an attack of glanders should consult two articles by S. H. Gaiger describing the course of the disease in his own person, and published in the

Journal of Comparative Pathology, 1913 and 1916. The first attack of the disease lasted for two years and a quarter, the second for a year and three quarters. In all, 82 operations had to be performed. Gaiger emphasizes the fact that in a pure glanders infection the bones are not attacked. It was only when a mixed infection with staphylococci developed that his bones and joints became involved. These two papers contain many useful suggestions regarding treatment. This is a striking example of recovery after a most severe infection, but the majority of cases eventually end fatally.

ACTINOMYCOSIS

Actinomycosis belongs to the group of the infective granulomata. It is caused by the actinomyces or ray fungus, which belongs to the group of the Streptothriceæ.

Bacteriology.—The actinomyces grows in the tissues in the form of little clumps or colonies, which are easily seen in the pus by the naked eye. These clumps are of a yellow color, and constitute the well-known "sulphur grain" bodies. When one of these bodies is crushed under a cover glass and examined unstained, three structures may be seen, filaments, spores or gonidia, and clubs. The filaments constitute the greater part of the body. In the center they form a dense felted mass. The spores are rounded bodies which are formed by segmentation of some of the filaments. The clubs are pear-shaped bodies which form a fringe round the periphery of the colony. They probably represent a means of defense against the protective forces of the tissues. The filaments and spores are Gram-positive, the clubs are Gram-negative. The organism only grows under anerobic conditions.

Fig. 25.—Grains of actinomyces from human pus; × 450. (Marwedel.)

The disease is common in cattle, occasionally affects horses, and is regarded as being rare in man. It is more than probable, however, as Cope points out in an excellent paper on the subject, that the principal reason for the apparent rarity in man is the frequency with which the diagnosis is overlooked. The disease may occur in the most unlikely situations and in the most atypical forms. Actinomycosis should always be considered in the diagnosis in the case of any newly formed subacute or chronic swelling, whether it appear neoplastic or inflammatory in nature, in the region of the mouth, face, neck, thorax, or right side of the abdomen.

The method of infection is still open to doubt. Direct transmission from an infected animal to man has never been proved. The com-

monly accepted view that infection is acquired through the eating of infected grain has little to support it, for the Actinomyces bovis has never been demonstrated on grasses and grains, although other microörganisms with somewhat similar characters have been described in these positions. It appears more probable, as J. H. Wright suggests, that the organism of actinomycosis is a true parasite and not a saprophyte, that it normally inhabits the alimentary canal, and that it enters the tissues through wounds, carious teeth, etc. Lord produced granulomatous lesions in guinea-pigs by inoculating them with scrapings from carious teeth and from the crypts of tonsils of persons free from actinomycosis, and these lesions contained granules composed of filaments and clubs apparently identical with those seen in actinomycosis. On the other hand most of the attempts to convey infection from human lesions to animals have been attended by failure.

The **sites of infection** are four in number. About 60 per cent of cases occur in the head and neck, 20 per cent in the gastro-intestinal canal—usually the region of the cecum and appendix—15 per cent in the lungs, and the remainder in the skin. In the cow the tongue is chiefly affected, giving rise to the condition known as "Woody tongue." Most of the cases in man originate in the mouth and pharynx, often in relation to carious teeth.

The streptothrix of actinomycosis exhibits some remarkable peculiarities in its **method of spread** which distinguish it from tuberculosis and syphilis, two conditions with which it is readily confused. Starting in the connective tissues, such as the subcutaneous, the submucous, the subperitoneal, and the subpleural, it extends by direct continuity. Apparently this extension occurs through some of the filaments being carried into the surrounding tissues, although by what means is at present unknown. Spread by the blood stream is uncommon, but a lesion may rupture into a vessel and give rise to metastases in distant organs. The liver, the brain, and the heart may thus be involved, and in rare cases the kidney, spleen, and ovary. Spread by the lymph stream is practically unknown, and the entire lymphatic system appears to enjoy a surprising degree of immunity, thus differing most markedly from its behavior in tuberculosis.

The **lesions** are similar to those of such granulomata as tuberculosis and syphilis, between which it is sometimes very difficult to draw a distinction. A firm mass slowly develops, which may retain its firmness for a long period, but finally softens and breaks down. The connective tissue, the muscle, and the bone are successively destroyed and replaced by granulation tissue which becomes riddled with abscesses. An abundant fibrous tissue reaction may lead to a brawny induration of the neck which may closely resemble sarcoma. The overlying skin becomes red and edematous, and may be perforated by the openings of numerous sinuses.

The pus is usually thin, and may contain the tiny yellow "sulphur granules," no larger than a grain of mustard, from which alone an absolute diagnosis can be made. These granules are most readily

found in the pus of a newly opened lesion. When the lesion has been discharging for some time it may be impossible to demonstrate them. In such cases it is best to allow a considerable amount of secretion to collect before examining it. The grains consist of a felted mass of mycelial threads at the periphery of which the peculiar club-like bodies can usually be recognized. The clubs are only found in the body, never being present in cultures.

In the *abdominal form*, which usually originates in the cecum or appendix, the chief growth is in the submucosa, in which flat gray nodules appear. In the course of time a large firm mass is formed, readily mistaken for malignant disease, and eventually suppuration converts the mass into a nest of abscesses. The abdominal wall may become

FIG. 26.—Actinomycosis. (Jacobi.)

involved, and a sinus discharges on the surface. The liver may become infected either by direct extension or by spread via the portal vein. A large honeycombed mass is formed which resembles a sponge saturated with pus.

The *lungs* are involved by extension downwards from the neck or upwards from the abdomen, although in some cases the infection appears to originate in a bronchus. The disease follows its usual course, so that the lung becomes riddled with abscess cavities, usually small and surrounded by abundant fibrous tissue. The condition may closely simulate tuberculosis, but as a rule the lower rather than the upper lobes are involved.

The **microscopic appearance** is that of a granuloma in which suppuration is frequently a prominent feature. The picture naturally varies much depending on whether suppuration has or has not set in. If the examiner is unusually fortunate he may find the masses of radially arranged branching mycelial filaments, around which is seen the usual collection of small round cells and mononuclears, whilst further out a well-marked fibroblastic reaction is evident. Giant cells may be present. Failure to find the mycelium in sections of the tissue is so frequent that it should never be accepted as a point of diagnostic value. For the same reason it is a mistake to excise a piece of the hard tissue

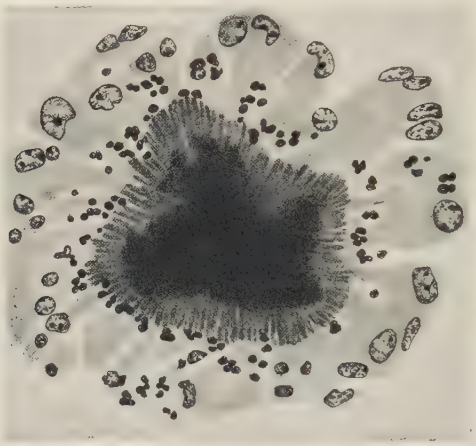

FIG. 27.—Actinomycosis bovis. Colony with clubs surrounded by polymorphonuclear and endothelial leukocytes. (Mallory.)

with a view to an examination for mycelia. When softening occurs they will be found infinitely more easily in the pus.

A word as to examining for the granules. The person with the best opportunity for finding them is the surgeon who opens the abscess. It is much better to pick out the granules and send them to the laboratory than to send a sample of pus taken at random. In the laboratory a good method is that advised by Colebrook. A few drops of pus are collected in a test-tube half full of water and fitted with a cork. The tube is shaken vigorously; the elements or ordinary pus are emulsified, whereas the sulphur granules are not broken up, sink to the bottom of the tube, and are easily recognized when the tube is held up to the light. A granule is transferred to a slide by means of a capillary pipette, lightly crushed under a cover glass, and examined unstained. The ray formation of clubs is seen between the surrounding pus cells and the core of the granule.

The course is very similar in whatever part of the body it occurs. First there is a firm tumefaction with no evidence of inflammation,

then areas of softening appear, and eventually the part may be riddled with sinuses. In the lower jaw the disease causes a brawny swelling which may extend down the neck, sometimes apparently severing its connection with the mandible. Abscess formation will probably occur sooner or later. In the next commonest site, the cecum, the chief growth is in the submucosa, in which flat, grey nodules appear. In course of time a large, firm mass is formed, readily mistaken for malignant disease, and eventually suppuration will riddle the mass with abscesses. Spread by the portal vein may lead to the formation of large, honey-combed masses in the liver, which may still further suggest the possibility of carcinoma. General symptoms of infection such as anemia, wasting, or fever, may be present in the later stages.

SPOROTRICHOSIS

During recent years a large number of cases of granulomatous infections caused by pathogenic fungi have been described, particularly in the United States. Of these two of the most important are sporotrichosis and blastomycosis.

Sporotrichosis is a chronic infection produced by a fungus of the genus Sporotrichium. The first case was described by Schenck in America in 1898. The fungus enters the skin through some abrasion, and sets up a slow inflammation which manifests itself in a series of gumma-like bodies, which break down to form abscesses, and these in turn may discharge on the skin as ulcers.

The *clinical differentiation* between this condition and syphilis or tuberculosis is often difficult and may be impossible. There is, however, something peculiarly suggestive about the gradual march of the disease up a limb along the line of the lymphatics, with here and there the development of a granulomatous mass. The fact that the disease responds well to iodide of potassium increases the confusion between it and syphilis.

Histological examination of the lesion is of no assistance. The picture is one of granulation tissue composed of fibroblasts, lymphocytes, epithelial cells, and giant cells. The latter are supposed to be characteristic, but in a typical case which I studied there were none present. Much, of course, will depend upon the stage at which the lesion is examined. When necrosis and suppuration sets in the picture will be much changed.

The only certain method of diagnosis is by *bacteriological examination* of the discharge from the lesions. The elongated spores of the fungus itself will not be found in human lesions, but a culture can readily be made upon ordinary agar, although a sugar-containing medium is even better. As the fungus grows well at room temperature, the whole proceedure can easily be carried out by a practitioner with a taste for bacteriology. The appearance in the course of a few days of a wrinkled pellicle which gradually darkens in color until it becomes black will prove an ample reward.

BLASTOMYCOSIS

Another inflammatory condition, at first granulomatous but later suppurative, is caused by the yeast-like fungi known as the Blastomycetes. The organisms, unlike the case of sporotrichosis, are found in the pus of the lesions. They are spherical bodies, somewhat larger than a red blood corpuscle, and present two characteristic features: (1) each organism is surrounded by a clear double contour, and (2) many of the organisms, like true yeast cells, show budding. The blastomycetes are best demonstrated by placing some of the pus on a slide, adding a drop of 10 per cent caustic soda, and examining the specimen unstained.

The **lesions** are usually confined to the skin, so that the condition is often known as blastomycetic dermatitis. They frequently follow a slight wound. At first they appear as papules, and throughout the disease the lesions are usually papillomatous in some part. In time they break down, become pustular, and ulcerate. The disease progresses over the skin, but as one part advances another part may heal. In this way large areas may in time be involved. The diagnosis from tuberculosis and syphilis is again often a matter of great difficulty, and has to depend on a demonstration in the pus of the infecting fungus. In some cases the fungus can be grown from the pus with considerable readiness on ordinary media at room temperature, but the demonstration of the spherical bodies in direct smears is the more satisfactory.

The **microscopic appearance** varies with the stage of the disease. In the early stage the picture is that of tuberculous granulation tissue with numerous giant cells, but later suppuration becomes quite marked. A noteworthy feature is the evidence of considerable epithelial hyperplasia on the part of the epidermis.

Occasionally it happens that the disease does not remain confined to the skin but invades the *internal organs*. As long as it is confined to the skin it is not dangerous to life, although of long duration. When it becomes generalized the termination is almost always fatal. It is by no means certain that the generalized condition is the same disease or caused by the same organism as the local one, but for a discussion of this problem treatises on bacteriology must be consulted.

The organs most frequently involved are the lungs, the muscles, and the bones, but almost any organ may be attacked, and a recent article described a case of blastomycosis of the brain. The pulmonary lesions are the first to attract attention, and the association of a skin affection with chronic pulmonary disease should suggest a search in the sputum for blastomyces. The lesions in the lung resemble bronchopneumonia or miliary tuberculosis, but cavity formation is uncommon. In bones the usual lesion is a suppurative osteomyelitis developing at the end of one of the long bones. Occasionally the vertebral column is affected.

In the generalized cases the microorganisms are usually present in large numbers, and they are three or four times the size of those

seen in the skin lesions. The histological picture in the internal organs is a combination of the granuloma formation and suppuration already described in the case of the skin.

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CHAPTER IX

HEMORRHAGE, THROMBOSIS, AND EMBOLISM

HEMORRHAGE

Hemorrhage may be due to three main groups of causes: (1) trauma, (2) pathological changes in the walls of the vessel, and (3) certain constitutional conditions.

It is the traumatic variety with which the surgeon is principally concerned.

The pathological changes in the walls may be patches of atheroma leading to cerebral hemorrhage; the lodgement of bacteria in the lumen of minute vessels causing weakening of the wall and it may be the formation of a mycotic aneurism with subsequent rupture; or the action of toxins upon the inner coat, producing cloudy swelling, fatty degeneration, and edema of the endothelium, as is so well seen in pernicious anemia.

The constitutional group is the most obscure. Doubtless in such conditions as Banti's disease and leukemia there is in addition a local change in the vessel wall. In such conditions, however, as hemophilia, vicarious menstration, etc. a local cause is hardly to be looked for.

The hemorrhage may be *external* upon a surface, or *internal* into the tissues. Internal hemorrhage may follow laceration of a vessel from trauma, and a large amount of blood may be poured into the tissues of a limb. The part becomes very dusky and swollen, and the circulation is interfered with so seriously through pressure on the veins that there may be danger of gangrene.

Hemorrhage is divided by the surgeon into primary and secondary. *Primary* hemorrhage occurs at the time of injury to the vessel. *Secondary* hemorrhage occurs at some later date, and is due to interference with the mechanism for the arrest of the hemorrhage. Such interference is usually due to bacterial infection.

The proteolytic ferments produced by the bacteria soften the newly-formed coagulum, and allow the hemorrhage to occur afresh. Secondary hemorrhage is rare in civilian work, but was extremely common in the recent war. From the pathological standpoint, however, the two conditions are identical.

The Arrest of Hemorrhage.—The *temporary* arrest of the hemorrhage is brought about by the formation of a clot, due to the coagulation of the blood. The *permanent* arrest is accomplished by the formation of an inflammatory exudate which in due time becomes firmly organized and seals the vessel.

Many secondary factors come into play, but it must be remembered that these are merely adjuvants to the essential phenomenon of coagulation, without which they are useless and without meaning. Of these secondary factors the more important are as follows.

1. When an artery is cut or still better when it is torn across, two phenomena occur, *retraction* and *contraction*. There is a large amount of elastic tissue in the inner coat and a certain amount in the middle coat of the smaller arteries. The recoil of this divided elastic tissue produces retraction of the inner and middle coats, so that these are drawn within the outer coat and the surrounding tissues, which thus form a sheath for the divided end of the vessel. The inner coat contains so much elastic tissue that it curls back into the lumen of the artery, sometimes completely blocking it. This mechanism is unable to come into play when an artery is only partially divided, under which circumstances it is best to make the division complete. A properly applied ligature acts in the same way; the inner and middle coats are ruptured and retract, and the constricted outer coat then closes the lumen.

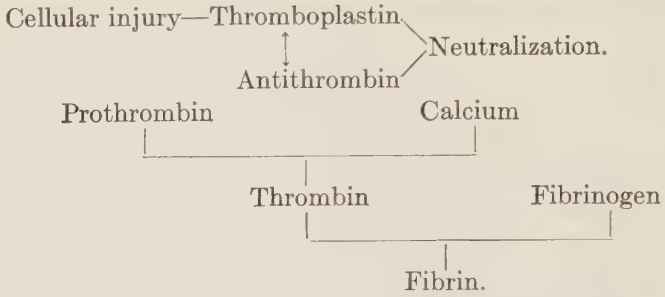
2. If the hemorrhage is sudden and severe there will be a great fall in blood-pressure, due to anemia of the vaso-motor center in the medulla. Such a fall will naturally facilitate the formation of an occluding clot in the vessel. The use of stimulants which will raise pressure and wash away the clot is therefore to be avoided.

3. To compensate for the loss of fluid in the vessels there is a great flow of lymph into the blood stream, partly from the lymphatics, partly from the tissue spaces. This favors the conversion of fibrinogen into fibrin, and therefore renders the blood more readily coagulable.

Formation of the Clot.—When blood is shed from a vessel, and especially when it comes in contact with injured cells, it clots. The *clotting of blood* is a complex process which is even yet not fully understood, but the recent work of Howell has thrown much new light on the subject. The coagulation of blood consists in the conversion of the soluble fibrinogen into insoluble fibrin. This conversion takes place owing to the action of a ferment called thrombin or fibrin ferment. The thrombin naturally does not exist ready formed in the blood, otherwise the whole blood would at once clot. It arises from the union of a previous substance, prothrombin, with the calcium salts normally present in the blood. It is here that Howell's views differ from those which previously held the field. It used to be taught that the prothrombin, derived possibly from the blood platelets, was activated by a previous substance thrombokinase, which was shed from the injured tissue cells.

Howell assumes that all the elements necessary for coagulation are already present in the blood, namely prothrombin, calcium, and fibrinogen, the prothrombin and calcium uniting to form the activating thrombin. The prothrombin is prevented from acting by the presence of antithrombin, the balance between the two being extremely delicate. Cellular injury liberates thromboplastin which neutralizes the anti-

thrombin. The prothrombin at once unites with the calcium to form thrombin, which in turn converts the soluble fibrinogen into insoluble fibrin. The reaction may be represented diagramatically as follows.



It will be seen that the key to the whole process is the injury of cells with the liberation of thromboplastin. If the blood be protected from the thromboplastin, clotting will be indefinitely delayed, a point of considerable practical importance. The blood in an isolated segment of vessel may remain uncoagulated for a long time, provided that the living endothelium has not been injured by the ligatures. When blood is collected for purposes of transfusion it is of great importance that it should be prevented from coming in contact with the tissues.

But although the clotting of blood is brought about by this delicate and ingenious mechanism, it does not constitute the only, or indeed the most important, means by which the hemorrhage is arrested. It plays an essential part in the formation of the temporary clot, but of only one variety of that clot, and it by no means the most important.

Two varieties of *temporary clot* are to be distinguished, the red and the white. The *red clot* is formed both outside and within the lumen of the vessel, and is the result of the process just described. It therefore consists almost entirely of fibrin containing red cells in the meshes of its network together with a few leucocytes. It is soft and jelly-like, and would never of itself be capable of effectively arresting the hemorrhage. It plays the part of a buffer, which serves to slow the flow of the blood, and thus allow of the formation of the much more efficient white clot.

The *white clot* is entirely different both in formation and composition. While the red clot is composed mainly of fibrin, the white clot consists almost entirely of blood platelets, with an admixture of a little fibrin and a few leucocytes. As the blood stream slows down the platelets fall out of the main current, and adhere to the injured end of the vessel, where they form a sticky white mass which acts as an effective cement to seal the injured vessel. This white clot formation, brought about by the conglutination of the platelets, is a more fundamental and primitive process than the formation of the red clot. It is found as a response to vascular injury throughout the animal kingdom, whereas it is only in the higher vertebrates that the

chemical formation of fibrin plays any part in the process of clot formation.

The temporary clot is now completed, and may be compared to a long nail, the head of which, formed mainly by the white clot but partly by the red, closes the end of the vessel, whilst the stem, represented by the red clot, occupies the lumen and may extend up the vessel to the nearest collateral.

The *permanent clot* is formed as the result of a process of plastic inflammation which commences shortly after the injury to the vessel. At the cut end of the vessel there occur those phenomena which have already been studied in our review of inflammation. An inflammatory exudate consisting mainly of lymph is formed, and soon becomes converted into granulation tissue by the ingrowth of new capillaries and fibroblasts. The temporary clot becomes vascularized and fibrosed in the same way, but shrinks considerably in the process, so that the internal clot may be represented merely by a thin fibrous cord. By this time, however, the end of the vessel is securely plugged by a mass of fibrous tissue, and the buffer action of the temporary clot is no longer required.

Before leaving the subject of hemorrhage brief reference must be made to the recent remarkable experimental work of Neuhof and Hirshfeld on the action of injections of sodium citrate upon the coagulation time of the blood. It was found that sodium citrate, which *in vitro* so efficiently prevents coagulation, when injected intramuscularly, intravenously, or subcutaneously produced prompt and pronounced shortening of coagulation and bleeding time. The action remains marked for two or three hours, and gradually passes off in the course of twenty-four hours. This effect is observed in patients with pathological prolongation of the coagulation time, as in jaundice. It does not occur in blood diseases such as hemophilia and purpura where there is a deficiency of platelets. If the work is confirmed its usefulness in cases where oozing may be expected during an operation is obvious. The intramuscular dose is 15 c.c. of a 30 per cent solution into each buttock.

THROMBOSIS

Thrombosis is the formation of a clot in the vessels or in the heart during life. It must be distinguished from the clotting of blood which occurs after death, or when the blood has been removed from the body. The one is an active process, the other is a passive one.

A *post-mortem clot* is seen typically in the heart after death. It is red, soft, friable, and is not attached to the heart wall. In many cases, however, although the lower part of the clot presents these characters, the upper layers may be tough and elastic, yellow in color, and of a translucent appearance. This is the so-called chicken-fat clot. The explanation of the appearance is simple. If clotting is delayed for some time after the circulation ceases the red cells will gradually settle to the bottom of the clot, where they form the ordinary red clot,

whilst the supernatent plasma coagulates to form the pale chicken-fat clot.

True thrombosis occurs when the blood is actually flowing. The result is the formation of a white clot or thrombus. The essential factor in thrombosis is an agglutination of the blood platelets, which adhere together at the point of formation of the thrombus and form ridges running at right angles to the flow of the stream. The surface of these ridges become thickly plastered with leucocytes. Moreover the platelets appear to liberate thromboplastin, whereby the neighboring fibrinogen is converted into fibrin which hangs in festoons between the ridges of platelets, entangling incidentally large numbers of red blood cells as they flow by.

A fresh thrombus, therefore, is made up of an essential basis of platelets, together with fibrin, leucocytes, and red blood cells. Disintegration of these various elements soon occurs, so that they come to form a homogeneous whole. The red cells lose their hemoglobin, and the color of the clot changes from red to yellowish grey. Such a clot may be distinguished from a chicken-fat post-mortem clot in that it is friable and granular, is not elastic, and when removed by force it leaves a dull and roughened surface on the vessel wall.

The factors which make for thrombosis are as follows:

1. Mere *slowing of the blood stream* will not of itself produce true thrombosis, but it acts as a very potent predisposing factor. This is well seen in the case of varicose veins, where the slow stream is so often associated with thrombosis, but where some other factor will always be found to be at work.

2. *Injury to the vessel wall* whereby the inner and middle coats are ruptured. This is made use of every day in the ligaturing of arteries or the arrest of hemorrhage by torsion of the vessel, procedures by means of which these two coats are torn and project into the lumen of the vessel.

3. *Contact with foreign bodies* or with any tissue uncovered by endothelium will give rise to thrombosis. A wire introduced into a vessel at once becomes the site of thrombus formation, and the same phenomenon is seen in the thrombosis on a roughened and bare patch in an atheromatous aorta or on an old vegetation on a heart valve. It is only the protecting endothelium that appears to be able to inhibit the ever-ready tendency towards thrombosis.

4. *Vascular obstruction* whether due to a ligature or to the pressure of a tumor depends for its effects upon whether it is partial or complete. If partial, a true thrombus may form. If complete, there will only be clotting of the blood.

5. *Inflammation of the vessel wall* is one of the most important causes of thrombosis, especially in veins. The inflammation may be an extension from without or may be due to infection in the blood stream. Examples of thrombosis occurring in inflamed veins are provided by varicose veins in the leg, inflamed hemorrhoids, the uterine veins in puerperal sepsis, the portal branches in an appendix abscess, the lateral

sinus in otitis media. It is not only in suppurative conditions that thrombosis may occur. Streptococci of low virulence may set up a chronic form of inflammation in the vessel wall, which sooner or later will be accompanied by thrombosis.

The relative importance of the two factors, slowing of the circulation and infection of the vein, has long been a subject of discussion. Virchow considered that thrombosis was the primary condition, and that any infection which might develop at the site of the thrombus was merely secondary. For long this conception of the so-called marantic origin of thrombi held the field. Welch, however, showed that the usual order of things is just the reverse; the infection occurs first, followed later by the thrombosis. Phlegmasia alba dolens of the puerperium is the classical example of this type of thrombosis, but similar thrombosis may occur in pneumonia, typhoid, erysipelas, tuberculosis, syphilis—indeed in nearly any acute or chronic infection. Moreover infective thrombosis may complicate such wasting diseases as cancer. In these cases it is exceptional to find the specific microorganism, such as the typhoid bacillus or the tubercle bacillus, at the site of the thrombus; the organisms present are usually secondary invaders, as a rule the pyogenic cocci.

Thrombosis, although an accompaniment of disease conditions, is nevertheless a protective mechanism. Without its aid we should bleed to death from every trival injury. It covers over a bare roughened patch on a vessel wall. It buries, to the best of its ability, a clump of bacteria on a heart valve under a mass of platelets, so forming a vegetation. It is true that at times the effects of thrombosis are unfortunate and undesirable, but such is only too often the case with the defense mechanisms of the imperfect body with which we still have to put up.

Venous thrombosis is very constantly accompanied by *edema* of the part involved. The leg may be swollen from the foot to the thigh. The explanation of this edema is not quite obvious. Ligature of the femoral vein at Poupart's ligament is unaccompanied by edema, provided that the lymphatics are left intact. When the large lymphatics are included, the result will be a marked edema. As phlebitis is so often associated with lymphangitis, it is probable that the edema of thrombosis is to be attributed to an accompanying lymphangitis.

A form of thrombosis of great interest to the surgeon is that which follows operations on the pelvic viscera, especially the uterus. The thrombosis is usually considered almost always to affect the femoral vein, particularly on the left side. Thrombosis of the pelvic veins, however, is much more frequent, although frequently overlooked, a point which will be discussed again in connection with pulmonary embolism. The thrombosis spreads from the uterine veins, or it may be the deep epigastric vein, to the external iliac, and thence downward to the femoral vein. Such a leisurely progress would correspond with the clinical course, for the symptoms do not as a rule appear before the end of the first or more usually the second week after the operation.

Subsequent Fate of the Thrombus.—After formation a thrombus contracts. It may then become absorbed or become organized.

Contraction occurs in every case, and is a phenomenon inseparable from the formation of fibrin. It is seen to best advantage when blood is collected in a wide test-tube; the clot shrinks away from the side of the tube, expressing in the process a large amount of serum. Similarly the clot in the vessel contracts. In doing so it may draw the vein wall with it, producing a puckering of the vein, or it may leave a space between the wall and the thrombus.

Absorption in part or in whole is of common occurrence. This is due to two main factors, softening and the activity of leucocytes.

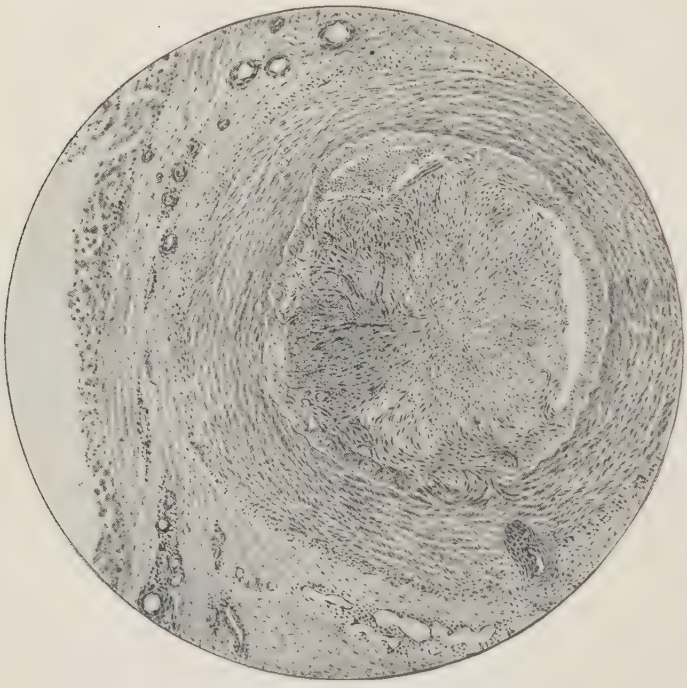


Fig. 28.—Thrombus undergoing organization. The clot is becoming vascularized and invaded by fibroblasts.

Softening of the center of the thrombus is probably due to lack of nourishment. Leucocytes play a most important part in the destruction of the thrombus, and are to be found in the clot in ever increasing numbers.

Organization of the thrombus occurs if absorption does not take place. From the spot in the vessel wall where the endothelium is injured there begins a peaceful invasion of vascular endothelium and fibroblasts, the process which has already been described at length in the chapter on Inflammation. Solid buds of endothelium grow into the clot, these become canalized, and form an interlacing network

of new capillaries. Fibroblasts grow in from the subendothelial connective tissue of the vessel, so that a vascular granulation tissue is formed. Later this becomes dense and fibrous, and the vessels disappear.

If the thrombus shrinks away from the vessel wall, as usually occurs, the vascular endothelium will cover it so that the lumen will be reëstablished. Occasionally, but rarely, the blood may tunnel through the thrombus, which thus becomes canalized.

Lime salts may be deposited in an old thrombus with the formation of a *phlebolith*. These phleboliths are found in varicose veins in the leg, and in the pelvic and prostatic veins. In these positions they often form very striking objects in X-ray pictures.

EMBOLISM

An embolus is a body which, after moving for some distance in the blood stream, becomes impacted in an artery or it may be in one of the branches of the portal vein.

In the great majority of cases an embolus is a thrombus originating in the veins, the heart, or the arteries. Occasionally, however, other substances may play the part of an embolus. Of these the most important are tumor cells, clumps of bacteria, fat globules, and air bubbles. They will be considered subsequently.

The two commonest sites from which emboli start are (1) veins—varicose veins in the leg, inflamed uterine and pelvic veins, an inflamed appendix, etc., and (2) the heart. In the heart the thrombus may be formed in the right or left auricular appendix, or it may be in the form of vegetations attached to the aortic or mitral valves.

An aseptic thrombus is only friable and liable to become detached and start on a journey in its early stages. Later it becomes organized and firmly attached to the wall of the vessel by the ingrowth of new capillaries and fibroblasts. It is in the early stages, therefore, that especial care must be exercised in handling the part.

A septic thrombus, on the other hand, is in a constant state of disintegration, and the danger of embolus formation is infinitely greater. The effects, moreover, of a septic embolus are proportionately more serious.

It is difficult to say in which organs emboli lodge most frequently. Pride of place must be given to the lungs, as emboli from the systemic veins are naturally first arrested there. Next we should probably place the muscles of the legs, for experimental observations have shown that particles of matter are usually swept past the openings of the great arteries passing to the viscera, and are carried into the iliac vessels. The resulting phenomena, however, are so slight compared with those seen in the brain, heart, spleen, kidneys, and intestines that attention is naturally focussed to an undue extent upon these organs.

Results of Embolism.—The effect produced by an embolus will depend upon: (1) The nature of the embolus, whether septic or other-

wise: (2) the extent of tissue affected, (3) the rapidity with which the obstruction is produced, and (4) the organ involved.

(1) *The Nature of the Embolus.*—When an *aseptic* embolus, such as may form in the auricular appendix, plugs a vessel the circulation is brought to a standstill, thrombosis occurs, and gradual organization of the thrombus ensures the completeness of the closure.

When, on the other hand, the embolus, derived from an inflamed vein or the vegetations of an acute endocarditis, is *septic* and contains masses of pyogenic bacteria, the sequence of events is very different. Such a mycotic embolus may give rise to a suppurative thrombo-arteritis which, extending in turn through the vessel wall, sets up metastatic abscesses. One of the most beautiful illustrations of this process is to be seen in the kidney in the case of miliary abscesses following an acute streptococcal endocarditis. One part of the arterial wall may become weakened and give way, with the production of a small mycotic aneurism which may subsequently rupture, a not infrequent cause of cerebral hemorrhage in young people.

(2) *The Extent of Tissue Affected.*—This is self-obvious and requires no elaboration. Obstruction of a small branch of the pulmonary artery may pass unnoticed, whereas death may follow blocking of one of the main divisions. If the main artery to a limb is blocked gangrene may result.

(3) *The Rapidity with Which the Obstruction Is Produced.*—This is a factor of considerable importance. If the blood supply to a part be gradually cut off, the vessels can adapt themselves to the changed conditions in time to save the life of the part. Sudden obstruction, descending like a bolt from the blue, catches the part unawares and the tissues rapidly die. The time during which the obstruction is maintained is also of great importance, but this hardly applies to the case of embolism.

(4) *The Organ Involved.*—It has already been remarked that although embolism of the muscles of the limbs must be common, it seldom gives rise to symptoms sufficient to attract attention. In such an organ as the brain, on the other hand, even a minute lesion may be attended by dramatic results.

It is the type of blood supply of the part, however, which is the most important factor in determining the extent of the lesion. Given an abundant collateral anastomosis the effect of the embolism may be negligible. So rapidly is blood poured in from subsidiary channels that the engine never falters in its stride. The ordinary skeletal muscles afford an example of such a collateral circulation. Some organs, of which the best examples are the lung and the liver, possess a double blood supply. In such an organ obstruction of a small artery will produce no effect. It requires the blockage of a large vessel to make itself felt. Given, however, a general circulatory disturbance of the part, such as chronic venous congestion of the lung, an embolus in a comparatively small vessel may cause trouble, because the collateral circulation cannot be efficiently established.

Infarction.—Other organs are unfortunate enough to receive their blood supply through a single artery. Such arteries are called "end arteries," and such a circulation is known as a "terminal circulation." Good examples of such an arrangement are provided by the kidney, the spleen, the branches of the internal carotid supplying the basal ganglia of the brain, and the central artery of the retina. When such an artery or one of its branches is blocked by an embolus, the corresponding area becomes acutely anemic and rapidly undergoes degenerative and necrotic changes. The process is called *infarction* and the affected area an *infarct.*

There are two great characteristics of an infarct: (1) death of the cells, and (2) coagulation, both intercellular and intracellular.

The part dies en masse, but the general architecture is not interfered with, the outline of the cells can still be made out, and the connective tissue framework remains intact. The life has gone out of the part, however, and one is reminded, as MacCallum puts it, "of the appearance of charcoal as contrasted with that of living wood, or of the streets of Pompeii as contrasted with those of a modern town." The cells may maintain an orderly arrangement, but it is a city of the dead.

Coagulation is brought about by the ferments liberated through the death of the cells. It affects the blood of the part, the coagulable fluid which flows into the part from the surrounding tissues, and the fluid within the cells themselves. It is the extensive formation of fibrin which is responsible for the swelling and firmness of the part. In the brain the liquefaction of the myelin counterbalances the firmness of the fibrin, and the part becomes soft.

Infarcts are usually classed as *red* or hemorrhagic and *white* or anemic. Although great stress is laid upon this differentiation, it is of merely secondary importance and is in no way an essential part of the process. When the part affected, usually wedge-shaped owing to the fan-like arrangement of the vessels, is deprived of blood the neighboring capillaries dilate and pour in blood, a praiseworthy but ineffectual attempt at establishing a collateral circulation. The vessels become stuffed with blood, and large numbers of red cells are found outside the vessels owing to diapedesis or in some cases rupture of the vessels. If the coagulation necrosis takes place before the hemorrhage occurs the infarct will be a white one, as in the kidney and spleen. In the lung, where necrosis is seldom complete owing to the double blood supply, the infarct is always of the red variety.

An infarct of the kidney or spleen becomes converted eventually into a mass of fibrous tissue, an infarct of the brain softens, liquefies, and gives rise to a brain cyst, but an infarct of the lung usually disappears entirely, so that an old healed pulmonary infarct is very seldom seen.

Pulmonary Embolism and Infarction.—The variety of infarction which is of more interest to the surgeon than all the others put together is infarction of the lung. The frequency of pulmonary complications

following more particularly abdominal operations is universally recognized. In a recent paper on ulcer of the stomach DeQuervain remarks that "three-fourths of the true post-operative deaths are due to lung complications—emboli, pneumonia, and lung gangrene." It has been the custom to consider a large proportion of these cases as infective in origin, and they are classed as post-operative pneumonia or ether pneumonia. Recent work, such as that of Wharton and Pierson, has shown conclusively that this view is erroneous, and that embolism and infarction account for the great majority of the cases. They consider that almost 50 per cent of the deaths after gynecological operations are due to this cause. Cutler and Hunt, from an exhaustive consideration of the statistics from some of the best hospitals, conclude

FIG. 29.—Large embolus in main branch of pulmonary artery. The embolus is seen as an oval body at the upper margin of the specimen.

that one in every 30 to 50 patients operated on, no matter what the anesthetic, develops a pulmonary complication, and one patient in every 150 to 175 dies from some such complication.

The embolus may originate in thrombosed veins in any part of the body, but most of the surgical cases are those in which a laparotomy has been performed, and operations for uterine fibroids, especially when a hysterectomy has been done, are particularly liable to be followed by this complication. This may be due to several factors, of which the three most important are laceration of the tissues, the

entrance of infection consequent upon opening of the vaginal vault, and the frequently dilated tortuous condition of the veins.

On clinical grounds we would say that the thrombosis following pelvic operations is commonest in the veins of the leg, the femoral and saphenous, particularly on the left side. It is well known, however, that with careful treatment such thrombosis rarely gives rise to embolism. Autopsy studies show that pulmonary emboli usually originate in thrombosis of the pelvic veins, a condition which as a rule entirely escapes clinical observation. It is more than probable that many obscure cases of fever during the second or third week of convalescence are due to pelvic thrombosis which may never draw attention to itself by terminating in pulmonary embolism.

FIG. 30.—Infarct of lung. The infarct is seen as a pale area surrounded by the darker zone on the left margin of the specimen.

The post-operative embolic phenomena may be divided into three groups.

(1) Cases of large emboli which occlude the pulmonary artery or one of its main branches, thus cutting off the blood supply to one or more lobes. A definite infarction does not result, but rather a widespread pulmonary edema without hemorrhagic consolidation. The

result is fatal in 90 per cent of the cases. The patient is suddenly seized with acute respiratory distress, and may die in the course of a few minutes.

(2) Cases of emboli of moderate size, leading to hemorrhagic infarction and consolidation with pleuritic symptoms such as pain, and signs such as a friction rub. The mortality is from 15 to 20 per cent.

(3) Cases of very small emboli giving rise to mild but characteristic symptoms, but with few or no physical signs. Wharton and Pierson observed no deaths in their series of cases.

Pulmonary infarction usually occurs during the second or third week of convalescence. Fatal embolism, however, may occur during the first two or three days. I once saw three such cases in the course of a month. Infarction occurring at this early stage is fatal in about 50 per cent of the cases. There is one sign which may put the surgeon on his guard; the second week of convalescence should be afebrile, but cases which are going to develop infarction show a slight but persistent rise of evening temperature during that period.

The onset of infarction is characterized by a sudden sharp pleuritic pain in the side. There may be hemoptysis, but this is by no means a constant feature. The temperature does not rise to any marked degree until the second day, and physical signs of consolidation do not appear for two or three days. All these features serve to distinguish the condition from a true infective pneumonia. X-rays may show the presence of an infarct even though all the usual physical signs are lacking. The first noticeable change is a clouding of the costophrenic angle, the rest of the lung remaining clear (Wharton and Pierson).

The infarct presents the usual cone shape, the base of the cone producing a slight elevation on the pleural surface. The customary site is the lower lobe. On section it is solid, dark red in color, and of a friable texture. An old infarct may become grey.

Microscopically the alveolar spaces are filled with red cells and are quite airless. Necrosis is uncommon, owing to the collateral blood supply from the bronchial vessels. For this reason also the infarct remains red, and does not develop into the white infarct seen in the kidney and spleen. Absorption of the smaller infarcts usually takes place in the course of two or three weeks, and the circulation becomes reestablished. When the infarction is due to infected emboli there may be abscess formation or gangrene of the lung.

Embolism of the Superior Mesenteric Artery.—Although of infrequent occurrence, embolism of the mesenteric vessels is so dramatic in its manifestations that it demands separate consideration. The embolus, which usually arises in the left side of the heart from vegetations on the valves or a thrombus in the auricular appendix, produces infarction of the bowel when it lodges in one of the larger branches of the superior mesenteric artery. Intestinal infarction may be caused by two factors other than embolism of the artery; these are thrombosis of the artery and thrombosis of the vein. Arterial thrombosis may usually be traced to atheromatous degeneration of the vessel wall.

Venous thrombosis is often associated with one of two conditions, acute appendicitis or acute inflammation of the female pelvic organs; the infection may, of course, come in addition from many other sources. The result of sudden obstruction of the vein is similar to that of sudden obstruction of the artery.

It may appear strange that a part in which the collateral circulation is so abundant should be subject to infarction. How is it that a circulation, which from the anatomical point of view is so rich in anastomoses, yet behaves as if it were a terminal one? It is because the sudden anemia produced by blockage of one branch of the artery sets up so violent a spasmodic contraction of the musculature of the bowel that the part becomes isolated from the neighboring circulation. Moreover this spasm aggravates the anemia to such a degree that death of the affected segment of the bowel speedily results.

The infarction, which is always of the red or hemorrhagic variety, usually affects the lower part of the jejunum and the ileum. There have been occasional cases in which embolism or thrombosis of the main artery has resulted in hemorrhagic infarction extending from the lower part of the duodenum to the transverse colon.

The affected portion of bowel is thickened, dark red in color, and soon becomes gangrenous. The limits are usually sharply defined, but the demarcation may be more gradual. The entire bowel wall is stuffed with blood, the mucosa is necrotic and may be ulcerated, the lumen contains thick tarry blood, the serous coat is covered by an inflammatory exudate, the peritoneal cavity contains bloody fluid, or there may be a general peritonitis. The mesentery is thickened and contains large patches of hemorrhage; the mesenteric veins are greatly engorged, and the mesenteric glands are swollen and hemorrhagic.

In some cases the degree of infarction is much less complete, and the hemorrhage may be confined to the mucosa. Occasionally the signs of infarction may be present although no obstruction can be found in the mesenteric vessels. In an autopsy on one such case I found a remarkable condition of large hemorrhagic patches through the lower part of the small intestine, although no lesion could be detected in the vessels.

Infarction of the intestine is not an invariable accompaniment of obstruction of the mesenteric vessels. Should the obstructed vessel be one of the smaller branches which anastomose freely with their fellows, the collateral circulation will be sufficient to prevent the development of infarction, unless, as has happened on rare occasions, numbers of the smaller vessels are blocked by multiple emboli. Slow obstruction of the vessels may also be unaccompanied by symptoms. A striking example of this has been recorded by Chiene, in whose patient, a woman sixty-five years of age, with marked arteriosclerosis of the abdominal aorta, there was complete fibrous obliteration not only of the superior mesenteric, but also of the inferior mesenteric and coeliac axis arteries, so that the blood supply of practically the entire intestinal canal had been cut off. The stomach and intestine appeared

quite normal, being supplied with blood by the greatly distended extra-peritoneal anastomosing arteries.

Obstruction of the inferior mesenteric artery is much less frequent than that of the superior mesenteric, nor is it so serious in its results, for the artery is not a terminal one, communication being established with the middle and inferior hemorrhoidal arteries below, and with the superior mesenteric above. In spite of this, however, obstruction is frequently followed by the production of a hemorrhagic infarct, but gangrene is not likely to develop.

The clinical picture is that of acute intestinal obstruction, the symptoms developing with great rapidity. The first symptom is sudden acute abdominal pain, due to spasm of the bowel from the sudden anemia. The pain, although constant, is marked by acute exacerbations, perhaps owing to the intestinal contractions. One of the most significant and suggestive symptoms is the passage of blood by the bowel, which may lead to a mistaken diagnosis of intussusception. Blood may also be present in the vomited material. At first there may be diarrhea, but this is followed later by complete obstruction.

Embolism of the superior mesenteric artery is fatal in the great majority of cases, even although the affected part of the bowel be resected. Should the obstruction be more gradual the termination may be more favorable. In such a case there may either be the establishment of a competent collateral circulation, with comparatively slight symptoms, or there may be intestinal infarction with varying degrees of damage to the bowel wall, but with ultimate recovery.

The other forms of embolism are not of sufficient importance to the surgeon to warrant more than a passing notice in this place.

Air may enter a vein if the great vessels at the root of the neck are wounded during an operation in that region, although it is probable that in the majority of such accidents the vessel has been torn between a ligature and the heart. The danger of air entering one of the smaller veins in the course of a transfusion has been grossly exaggerated. I know of a surgeon who in the early days of salvarsan administration inadvertantly pumped a large quantity of air into the median basilic vein without producing any unpleasant results. In the fatal cases the air either forms a froth with the blood in the heart, upon which the heart is unable to contract, or it gives rise to numerous air-emboli in the capillaries of the brain.

Fat emboli enter the blood stream as the result of fracture of the bones with laceration of the marrow, or they may follow convulsive seizures, or even a severe blow. The fat globules can be seen distending the pulmonary capillaries, and appearing as highly refractile bodies which stain red with Sudan 111. Animal experiment has shown that the condition is not nearly so serious as used formerly to be supposed. Indeed it is probably of little significance.

Tumor cells may be carried in clumps along the blood stream and stick in a vessel, but, although they result in metastases, they seldom give rise to the ordinary phenomena of embolism.

Bacteria circulating in clumps behave very much as tumor cells. They may set up metastatic abscesses, but there are none of the signs of vascular obstruction.

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CHAPTER X

SURGICAL SHOCK

The subject of shock is one which has exercised the medical profession for many years, more especially since the development of abdominal surgery, for it still presents what is perhaps the greatest menace to abdominal operations. Interest in the condition has received an enormous impetus recently on account of its extreme frequency as a complication to wounds. A very large volume of clinical and experimental work has been put on record during the last few years, some of the most important of which may be found in the special reports of the Medical Research Committee on Surgical Shock. Even yet, however, although great advances have been made, and many theories previously held have been exploded, it cannot be pretended that the mystery has been finally solved.

A patient in a condition of profound shock presents a very *characteristic appearance*. He lies perfectly still, and pays no attention to what is going on around him. The face is overspread by an ashen-grey pallor, large drops of sweat hang from the eyebrows, the eyes are weary, lusterless, and deeply sunken in their sockets, the cheeks hollow, the brow furrowed with anxiety, the skin cold and clammy. Four of the vital processes are notably depressed: (1) the temperature is subnormal; (2) the pulse is extremely feeble, running, and irregular; (3) the respirations are shallow and sighing; and, most important of all, (4) the blood pressure falls very low. Although plunged in mental torpor the patient is quite conscious and answers questions slowly, painfully, but correctly.

In seeking for an explanation of this peculiar and ominous condition the mistake has perhaps been made of supposing that one and the same fons et origo mali is responsible in every case. It is almost certain that the reverse is true, and that, just as many and varied factors may give rise to heart failure with its constant clinical picture, even so numerous and varied may be the conditions which result in shock.

Shock may be primary or secondary. *Primary shock* is the immediate result of some severe trauma. *Secondary shock* is a condition which comes on some twenty-four hours later, and was the variety usually seen in the war.

Causes.—Although in experimental work shock may be due to a single cause, in actual practice it can almost always be traced to a variety of factors, and this multiplicity of causal agents adds seriously to the difficulties of study. Of the factors which may induce shock the following may be mentioned.

1. *Severe Blows on the Chest or Abdomen.*—At the autopsy no gross lesion may be found, and yet the shock may have been so profound as to terminate in death.

2. *Manipulation* of the viscera, the mesentery, and the parietal peritoneum during abdominal operations. One of the most important causes of shock in civil practice is undue exposure and handling under anesthesia of the unconscious and unprotesting abdominal organs. Shock due to intussusception or a strangulated hernia comes into this class.

3. *Extensive Burns of the Skin.*—It is the extent rather than the depth of the burn which is of account.

In these three groups of cases the natural explanation to suggest itself is that the nerve centers, especially those vital centers situated in the medulla, are bombarded with impulses due to the excessive stimulation of the peripheral nerve endings, as the result of which a state of exhaustion or inhibition may supervene.

4. *Hemorrhage.*—Hemorrhage and shock are usually combined in actual practice, and it is difficult to separate them and to determine to which factor the symptoms are mainly due. Severe hemorrhage itself may produce all the phenomena of shock. In addition it is capable of producing physical changes such as chromatolysis of the nerve cells in the medulla and cerebellum which are supposed by some to be characteristic of shock. The mere fact that the vessels are comparatively empty of blood is quite sufficient in itself to produce a condition of shock; indeed this is the very essence of the condition.

5. *Obstruction of Vessels.*—Erlanger and his associates have shown that a shock-like condition may be produced in animals by obstructing the aorta or the inferior vena cava. The result is the same as in hemorrhage, an emptying of the arterial system.

6. *Bruising of Muscles.*—Bayliss and Cannon have shown experimentally that severe laceration and crushing of muscles are followed by the development of a typical shock-like condition. If a ligature be kept on the main vessel of the limb and the limb be amputated no shock will develop, showing that the shock was not due to afferent nervous impulses, but to the absorption of toxic products into the circulation—an aseptic traumatic toxemia. Injection of extracts of the crushed muscles produces the same effect. The application of a tourniquet proximal to the injured part may be followed by marked improvement. This fundamentally important observation strikes a death-blow at some of the theories of shock held hitherto, and it affords a satisfactory explanation of many of the cases of secondary wound shock seen during the war.

7. *Injection of Histamin.*—Throwing an interesting side light on the phenomena described in the previous paragraph is the recent work of Dale and Laidlaw, who showed that the injection of the base histamin will lead to a condition closely resembling shock. There is the characteristic fall of blood pressure which is due, not, as might be supposed, to failure of the heart and dilatation of the arteries, but

to a paralytic dilatation of the capillaries. Histamin was extracted by Dale from ergot, but Abel has found that he can extract it from practically every tissue, so that it or some closely allied body may be the actual substance concerned in the crushing experiment.

8. *Infection.*—It is well known that certain acute septic conditions such as acute pancreatitis are accompanied by shock. Very many cases of delayed shock during the war, in which the symptoms came on 12 or 24 hours after the receipt of the wound, were due to acute streptococcal infection or to commencing gas gangrene. The widespread removal of lacerated muscles and even the early amputation of a limb, which undoubtedly greatly reduced the amount of shock and which was adduced by some as proof of the theory of the absorption of the products of muscle autolysis, was beneficial on account of the much needed removal by this means of an extensive focus of septic infection. At the same time it is open to question whether it is justifiable to consider what is really a state of toxemia as being synonymous with true shock. The collapse in severe diphtheritic and other infections is not regarded as shock, however closely the phenomena of the two conditions may resemble one another. It has been well said that shock is essentially a temporary condition, a step towards death, but a step which the patient may retrace in a few hours, whereas recovery from sepsis may take weeks or months.

As a matter of fact, although it is possible in the laboratory to try out each individual factor separately, it rarely happens in actual practice that only one factor is involved. For instance trauma, laceration, hemorrhage, and infection, are frequently combined.

Moreover, accessory factors may play an important part. Cold, exhaustion, and depression predispose to the occurrence of shock. It has been said, with what truth it is difficult to determine, that shock is more common after a lost battle than after a victory. Anesthesia plays an important part. Ether and chloroform anesthesia are certainly more dangerous in this respect than nitrous oxide-oxygen anesthesia. It may be wise, therefore, in cases where bacterial or other toxemia plays an important part to avoid chloroform and ether.

Theories of Shock.—A consideration of the varied nature of the foregoing factors will render it easy to believe that we are not by any means dealing with an identical condition in every case that is labelled shock. And yet in very many cases so constant a picture as that made up of collapse, subnormal temperature, very low blood pressure, and failing pulse and respiration may well have some constant pathological basis. What then is the most probable explanation of this series of phenomena?

The theory which, until the recent work during the war, was almost universally accepted was that proposed by Crile many years ago to the effect that the factor of prime importance was *paralysis of the splanchnic vessels,* as the result of which the rest of the body was bled into the splanchnic veins. It did not take long to discover,

however, that in the wound-shock cases there was no enlargement of the splanchnic vessels.

Paralysis of the vasomotor center has been suggested, owing to the extreme fall in blood pressure. But it is now known that not only are the arteries not dilated in shock, they are actually contracted. Moreover the superficial veins are also so contracted that in some cases it is only with the greatest difficulty that a cannula can be inserted for the purpose of blood transfusion. When we consider that one of the fundamental findings in shock is the emptiness of the larger vessels, it is but natural that the vessel walls should endeavor to narrow the lumen to as great an extent as possible.

The *acapnia* theory of Yandell Henderson depends on the fact that the one great stimulant of the respiratory center is the presence of carbon dioxide in the blood. The painful stimuli cause rapid though shallow respiration, as the result of which so much carbon dioxide is given off from the body that the respiratory center loses its customary stimulus, ceases to function, and the patient suffers and perhaps dies from lack of oxygen. On account of the lack of oxygenation a condition of acidosis develops. Such a theory would be difficult to accept unless overwhelming proof could be brought forward in its favor.

Fat embolism affecting the lungs and the brain has been suggested as being a factor of importance. Porter in particular has pointed out that shock is specially common in fracture of the femur and extensive wounds of the subcutaneous fat, conditions in which fat particles may readily enter the blood stream. In such cases he claims to have demonstrated fat globules in abundance in the lungs. It is perfectly obvious that such an explanation is quite inadequate in many cases of shock, those for instance in which the condition is due to exposure and handling of the abdominal viscera.

Capillary Paralysis.—The fundamental condition in all varieties of shock appears to be the empty state of the vessels. The heart has not sufficient blood upon which to contract, and the vital as well as the higher centers suffer acutely from lack of nourishment. By employing the vital red method it can be shown that the total volume of blood in active circulation is greatly diminished. If, then, the blood is not in the arteries or in the veins, where is it? It has collected in the great capillary bed, and much of it is in a veritable backwater. Under normal conditions the capillary bed is only partly used, and many capillaries which are usually collapsed now become distended with blood owing to a *universal loss of capillary tone.*

At the same time there is an *increased permeability of the capillary walls,* so that a considerable quantity of fluid passes out into the tissues, although not sufficient to produce edema, with the result that the blood becomes concentrated. When a shocked patient is transfused with saline a large part of the saline passes from the capillaries into the tissues in the space of half an hour. For this reason Bayliss has suggested the use of a colloid such as gum acacia, the molecules of which are

too large to escape through the vessel walls. A 6 per cent solution of gum acacia in normal saline is injected intravenously. No method, however, is so beneficial in this respect as transfusion with whole blood.

To what is the widespread capillary paralysis due? That is a question to which at the present moment an answer can hardly be given with confidence. It appears difficult, however, to escape from the admission that it is due to the effect on the brain of the abnormal impulses, whether nervous or toxic, which are playing upon that organ. Long ago Crile pointed out that chromatolysis, eccentricity of the nucleus, and other evidences of nerve cell exhaustion could be demonstrated in the brain, and more particularly in the cells of Purkinje in the cerebellum, but similar changes may result from hemorrhage without any attendant shock. Rendle Short in a recent paper has thrown further light on this subject. In cases of wound shock in the war he found loss of Nissl's granules, etc., in the sensory nuclei such as the gracile and cuneate nuclei in the medulla or the optic thalamus, whereas the motor cells in the cerebral cortex, the lenticular nucleus, and the motor nuclei in the medulla showed no alteration. These results, if confirmed, seem to suggest that the sensory side of the brain bears the brunt of the attack, and that the capillary paralysis is a reflection of the resulting exhaustion. It must never be forgotten, however, that all of these changes in the brain may be the result and not the cause of shock, and that the key to the mystery may still to be discovered.

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CHAPTER XI

TUMORS

A tumor is a growth of new cells which proliferate without control, and which serve no useful function. It is therefore called a new growth or neoplasm. Many new formations occur in the body which are not true tumors; the callus following a fracture of bone, the physiological hypertrophy of the breast and uterus, the granulomatous masses characteristic of syphilis and tuberculosis. It is probable that some conditions at present regarded as tumors may later be recognized to be due to some other cause.

ETIOLOGY

What shall be said regarding the cause of tumors? When the truth is admitted we have to confess that the essential cause is still completely unknown; the veil covering the mystery has not yet been rent in twain. Theory after theory cometh up as a flower, only in turn to be cut down like the grass. Yet it is permissible to make some guesses at the truth, although the history of oncology is strewn with such broken fragments. Cohnheim's theory of embryonic rests, Ribbert's theory of tissue-tension, Adami's theory of habit growth, all of these describe circumstances which may prove favorable to increased cellular activity, but they do not suggest what is the actual stimulus responsible for this activity. Certain conditions may be more favorable than others to the ovum, but it is only the stimulus of the spermatozoon which starts it on its course of limitless proliferation. It has been said that a chorionepithelioma is merely the expression of abnormal activity on the part of the fetal trophoblast. But such a statement in no way explains why anarchistic tendencies should occasionally be displayed by cells which under ordinary circumstances are subservient to strict laws. As Emery remarks, it is as if a peaceful herd of cows, accustomed to browse quietly on the pasture, should suddenly begin to burrow into the ground like rabbits. Some very real additional factor must be present, and not merely a slight excess of a normal physiological tendency.

The idea that the unknown stimulus may be due to the action of some hitherto undiscovered microorganism receives scant attention in most text-books, but no absolutely conclusive argument can be urged against it, and Emery has recently pointed out how very much may be said in its favor.

The microorganism must be so small as to escape detection, but this is true of many of the filter-passers. It must inhabit the cell, and multiply within it, so that when the cell divides each of the

daughter cells is also infected. It must produce a toxin with the power to induce cell division.

If each cell contained only one microbe it would be difficult to conceive how both should subdivide at the same moment. But there is no reason why there should be only one. The pus cells in gonorrhea, the specific cells in rhinoscleroma, are loaded with bacteria. In tropical sore a single cell may contain from 100 to 200 organisms.

The production of cellular proliferation by bacterial toxins may be observed in any case of chronic inflammation. The formation of giant cells in tuberculosis affords a familiar example of this process. Scharlach R when applied to an epithelial surface causes a continuous proliferation of epithelial cells which may bear a strong resemblance to the proliferation seen in an epithelioma. Even more striking than the action of Scharlach R on epithelium is the recent experimental production of carcinoma by the application or the injection of tar. Granted a bacterium which has a continuous stimulating influence on epithelium like Scharlach R, and provided it can live and multiply in a cell, the result will be a neoplasm.

Many conditions now known to be infectious in nature can with difficulty, if at all, be distinguished from true neoplasms. Warts are known to be due to an infection, they can be inoculated from one person to another, and yet they are identical both macroscopically and microscopically with a papilloma. Molluscum contagiosum is due to an unknown filter-passing organism, but it bears the closest resemblance to an innocent epithelial tumor. And who shall say either from the histological picture or the clinical course whether Hodgkin's disease should be regarded as a neoplasm or as one of the infective granulomata? Coccidiosis of the liver of the rabbit produces an appearance identical with that of a complex papilloma such as a papillary tumor of the bladder, so that if the cause were not known to be a protozoon the condition would be regarded as a true neoplasm. The infective (venereal) sarcoma of dogs is histologically a true tumor, a round celled sarcoma, but it is certainly infectious in nature. Rous' chicken sarcoma (see page 166) probably belongs to the same category. Vegetable galls, which are organized structures rather than mere masses of hypertrophied tissue, are due to the action of a toxin injected by an insect when the embryo is deposited. Indeed all the principal features of true tumors can be paralleled by plant conditions which are known to be due to parasites. The researches of Erwin Smith have shown that when the proper species of plant is inoculated with Bacterium tumefaciens of crown gall, a growth will result which bears a strong resemblance to mammalian cancer. Moreover, the secondary growths which develop are not produced from the tissues where they are found, but from that of the primary tumor. A secondary growth on a leaf is composed of root cells if the primary growth arises in the root, or of stem cells if the growth begins on the stem.

The common sites of tumor growth appear to point to a possible bacterial cause. The parts of the body liable to infection are the com-

mon sites of primary tumors. The mouth, the stomach, the rectum, the uterus, the breast, all in free communication with the exterior, are the most frequent sites of carcinoma. The small intestine, the urinary bladder, and the gall bladder, in which the communication is less free, are less commonly affected. The relation between gall stones and carcinoma, and between gall stones and infection, is well recognized. Such organs as the spleen, the liver, the brain and spinal cord, the heart, and the muscles, all more or less isolated from the exterior, are rarely the seat of primary growths. Yet the liver possesses no natural immunity, for it is one of the organs most frequently affected by secondary growths. It is curious to recall that tumors of ciliated epithelium (nose, bronchus, Fallopian tube, vas deferens,) are extremely rare, while tumors of all other kinds of epithelium are equally common. May it be that these ciliated cells are better able to protect themselves from invasion?

Ochsner has recently called attention to some racial characteristics which are of interest. Cancer of the stomach is very common in what he calls manure-eating peoples. It is common, for instance, amongst the Japanese who eat raw vegetables grown in soil fertilized with human or animal manure. It is remarkably rare in India, where their religion makes the people boil their food and drink. On the other hand the Japanese, who are scrupulously clean and wash in hot water, are singularly free from cancer of the skin, a condition which is very common in India where the skin is frequently very dirty. Cancer of the stomach is very rare in the tropics, except where vegetable gardens are conducted by the Japanese and Chinese. In the tropics human excrement is not needed to fertilize the soil. Gastric cancer is common in manure-eating animals, such as fowls and pigs. Marine and Gaylord have shown that fish living in ponds infected with feces develop cancer of the gills, whereas control fish in pure water do not.

Dolbey and Moore in a recent study of malignant disease in Egypt point out that there is practically no cancer of the stomach in that country, and that cancer of the large intestine is very rare in spite of the universal parasitic infections of the colon. They note that the diet of the fellaheen is almost entirely vegetarian. Meat is eaten only once a week, and cheese, milk, eggs and beans form the most important part of the daily diet. Epithelioma of the scalp, on the other hand, is much more common than in England and America, a fact which may be explained by the habit of shaving the head, and the intensity of the actinic rays of the sun.

It may be urged that if tumors are infectious in nature, they may be transmitted from one patient to another. But a slight knowledge of the history of medicine will show that there may be nothing so difficult as to prove the communicability of a disease. As late as 1891 one of the standard text-books of medicine stated in the most categorical manner that phthisis could not possibly be an infectious disease. What case is known of a carbuncle being communicated from one person to another? Yet it is certainly bacterial in origin. Moreover the possi-

bility of cage infection in laboratory animals appears to be definitely proved. Cages which have been inhabited by cancerous mice show an undue proportion of positive cases. Loeb has recorded three cases of cystic sarcoma of the thyroid developing in rats in adjacent cages, an occurrence all the more extraordinary when it is recalled that spontaneous tumors in rats are very rare, and that this variety of tumor is even more so.

The object of the above discussion is not to imply that the evidence in favor of the bacterial causation of tumors is in any way overwhelming. There are many grave difficulties which could readily be urged. It is merely intended to point out that there is more to be said for this view than is usually admitted in text-books of pathology, and that the only wise course is to maintain an open mind.

Of the *predisposing causes* the only ones of importance are irritation and age.

Irritation, usually of some duration, precedes a large number of cases of cancer. Indeed it is almost permissible to say that cancer does not develop in a healthy tissue, but in one whose resistance has already been weakened, usually as the result of chronic irritation. Innumerable examples of this truth could be given. Cancer of the lip is usually associated with heavy pipe smoking, cancer of the tongue and cheek with a jagged tooth. Cancer of the gall bladder is much commoner when calculi are present. Cancer of the cervix uteri occurs in women in whom the cervix has been lacerated as the result of childbirth. Chimney sweepers, paraffin workers, and workers with aniline dyes are liable to develop cancer on that part of the skin exposed to the irritant. An X-ray burn, and indeed any old burn, may become the starting point of a cancer. A chronic ulcer whether of the tongue, the stomach, or the leg, may develop into a malignant growth. The natives of Kashmir wear a hot basket of charcoal, the kangri, under their clothes for purposes of warmth, and cancer of the abdominal wall is common amongst them, whereas it is almost unknown in other races. Chronic mastitis is very frequently associated with cancer of the breast.

In all of these cases the irritation is of a prolonged and chronic character. Occasionally a sudden trauma may be followed by the development of a malignant growth. Sarcoma of bone may develop at the site of a contusion, cerebral tumor may follow a head injury. The injury, however must be slight—a contusion and not a fracture. This holds true also in the case of tuberculosis and hematogenous osteomyelitis. Apparently the violent reaction which occurs at the site of a fracture results in a local immunization by cells and body fluids which is sufficient to prevent the operation of any extraneous factor.

It will be noticed that in every one of the instances of chronic irritation, the irritation preceding the cancer occurs in a region very liable to infection. If cancer is due to a parasite it may be said that

man is relatively resistant to that parasite, so that in most cases the predisposing cause, such as irritation, must act for a long time.

Although statistics are so notoriously untrustworthy, yet it does appear to be the case that sarcoma is frequently preceded by a blow on the affected part. This is particularly well seen in sarcoma or glioma of the brain, a subject which will receive fuller discussion in Chapter XXXI.

Age appears to play some part as a predisposing cause. Many tumors have a characteristic age distribution. Uterine fibroids occur during the child-bearing period, angiomas are congenital, cancer is rare before the age of 35, bilateral sarcoma of the kidney and neuroblastoma are confined to early life, and so on.

INNOCENT AND MALIGNANT TUMORS

There are two great classes into which tumors may be divided, the innocent, simple, or benign, and the malignant. The typical examples can be differentiated at a glance. Between these two extremes, however, there are intermediate grades, especially in the connective tissue tumors, which renders a hard and fast line of demarcation impossible. It is not possible at present to say whether an innocent tumor ever becomes converted into a malignant one. Certainly the clinical evidence points that way, as in the transformation of a papilloma of the skin, bladder, or rectum into a carcinoma, a pigmented mole into a melanotic sarcoma, or an apparently innocent fibroid of the uterus into a malignant tumor, but it is more than possible that these tumors have been really malignant in type from the beginning, and are merely entering on a period of increased activity.

A malignant tumor differs from an innocent one in the following particulars:

1. It kills the patient wherever it may grow. An innocent one is only dangerous to life when growing in some vital part, such as the brain or larynx.

2. It infiltrates and destroys the surrounding parts. An innocent tumor merely pushes them aside, compressing them so that a capsule is formed. An angioma or glioma, however, may infiltrate widely.

3. It sets up secondary growths or matastases in neighboring lymphatic glands and in distant parts of the body, being spread by the blood stream or the lymphatics.

4. It tends to recur locally after removal. This, however, is merely because the removal has not been sufficiently wide.

5. It fails to approximate in character to the tissue from which it grows, rather resembling, especially in the connective tissues, the embryonic type. The innocent tumor reproduces the normal adult structure.

6. It usually shows mitotic figures. These are very rare in innocent tumors.

7. Its growth is usually rapid. It may however be very slow.

Autonomy.—Perhaps the most characteristic feature of tumors, seen to better advantage in the malignant than in the innocent variety, is their autonomy. The cells are not governed by the laws of the body in their growth. They are the Bolshiviki of the body, for they know no law, pay no regard to the common weal, serve no useful function, produce disharmony and destruction in their immediate surroundings, and scatter the seeds of future trouble in distant parts. A tumor does not share with the other tissues the varying fortunes of the body. The patient may be wasted with tuberculosis, but a lipoma refuses to give up its fat. A huge sarcoma may flourish exceedingly upon a wretch whom it has reduced to a mere shadow.

SPREAD OF TUMORS

An innocent tumor grows by expansion, much as a football grows when filled with air. A malignant tumor may spread in three ways: (1) by infiltration, (2) by embolism, and (3) by transplantation.

1. **Infiltration.**—This may occur in two ways.

(*a*) *Infiltration into Tissue Spaces.*—The tumor cells extend outwards between the planes of fascia, between muscle fibers and fat cells, and the mass comes to assume in consequence a very irregular form.

(*b*) *Permeation of the Lymphatics.*—Sampson Handley has shown that in the breast at least this is a very common method of spread. Tumor cells enter a lymphatic vessel and grow along it. Their presence produces an inflammatory reaction around the vessel, evidenced by a collection of lymphocytes and fibroblasts. This reaction may finally obliterate the vessel and choke the tumor cells, the whole becoming converted into fibrous tissue. The growing tip of the process is left and may thus appear quite isolated from the parent mass. Extensive spread may occur in this way, the lymphatics in a wide area of skin surrounding the tumor may become infiltrated, and a carcinoma of the breast may reach as far as the liver. Cancer of the uterus may extend in a similar manner.

2. **Embolism.**—Emboli of tumor cells may be carried by the blood stream or the lymphatics when the growth has invaded the respective vessels. The former method is common in sarcoma, the latter in carcinoma. A carcinoma, however, is not infrequently distributed by the blood.

The emboli settle down in distant organs or lymph glands and set up secondary growths or *metastases*. The lungs for the systemic, the liver for the portal circulation, are naturally the two organs most frequently involved. It is often very difficult to explain the distribution of metastases. Organ predilection may play an important part. Although large numbers of emboli must lodge in the muscles, yet they do not produce secondary growths. They must be killed off, or fail to find a suitable environment. Sometimes one tissue is picked out in a remarkable manner. Thus cancer of the prostate, breast, thyroid,

kidney, and adrenal (hypernephroma) tends to set up widespread secondary growths in bone. Organs liable to primary cancer, as the breast, uterus, and stomach are rarely the seat of secondary growths. In those in which secondary growths are common, as the lungs and liver, primary growths are rare. Some organs, such as the heart and spleen, although provided with an abundant blood supply, are seldom affected by either primary or secondary tumors.

3. **Transplantation.**—This is not a common method of spread, but in a serous cavity the route by which the tumor cells have been carried from one place to another may be very evident. In one case of cancer of the stomach there were large secondary growths in both ovaries (Fig. 200, page 524), and the intervening peritoneum was studded with small nodules similar in structure to the growths in the stomach and ovaries. Undoubted cases have occurred in which a tumor of the lower lip has been transferred to the upper, or one of the cervix to the opposite wall of the vagina.

Inoculation is one variety of transplantation. It is well recognized by surgeons that if a tumor be cut into during the course of its removal there is danger of infecting the surrounding tissues and the skin. That this danger has been overestimated has been shown by the recent experimental work of F. C. Wood, but Kettle records a case where an exploring needle was passed into an adenocarcinoma of the liver, and a few months later a nodule with the same structure appeared in the skin at the site of puncture.

GENERAL SIGNS OF MALIGNANCY

The patient suffering from malignant disease sooner or later displays general constitutional signs of his malady. It is remarkable, however, how long in some cases the general health may be unimpaired. The most striking case which has come under my own observation presented the following remarkable history. The patient, a healthy farmer 38 years of age, had a mass removed from the right axilla in March, 1918. It had been there since the middle of the previous year, but did not trouble him at all. Microscopic examination showed it to be a typical melanotic sarcoma containing a large amount of pigment. He made a rapid recovery, and did a full summer's work on his farm. In the autumn several dark nodules appeared on the skin of the chest and anterior abdominal wall. These were excised, and proved to be identical in structure with the mass from the axilla. His health remained unimpaired but realizing the seriousness of his condition he insured his life as a first class risk.

In June, 1919, he reappeared in hospital with an acute intussusception. At the operation an enlarged gland was found adhering to the bowel at the site of the intussusception, and was probably the cause of that condition. Sections showed the structure which had already become so familiar. In September he presented himself again, this time complaining of sore throat, and it was found that the tonsils were converted into two large black masses. These were removed, and

needless to say they were the seat of melanotic sarcoma. He returned to his farm and continued to work throughout the winter, but in the spring he succumbed rather suddenly, the exact details not being available. He thus enjoyed three years of robust health, although he must have been riddled with melanomata, and he actually passed for life insurance.

Emaciation is one of the constant accompaniments of malignant tumors. Its exact cause is not understood. Several factors may be at work. Thus in cancer of the esophagus and stomach starvation plays an important part. It chiefly affects the muscular system, and in some cases the fat deposits are little altered. It is preceded by muscular weakness.

The *blood* usually shows a change in the red cells, and occasionally in the white. The common change is a secondary anemia, with diminution in the number of the red cells, but a greater fall in the hemoglobin, a low color index, and a slight leucocytosis. In cancer of the stomach the anemia may be the dominant feature, and may be of the pernicious type. The chief cause of the anemia is hemorrhage, and the absorption of hemolytic substances from ulcerating surfaces. These circulating hemolysins may be a source of danger in blood transfusion. The red cells are hemolyzed by normal blood serum, a fact which has been utilized as a laboratory test.

Leucocytosis is present in many cases, but is probably to be attributed to the accompanying sepsis, as it does not occur in uncomplicated cases. In severe cachexia with anemia there may be myelocytes in the circulating blood, together with nucleated red cells.

Sepsis is a very important factor in malignant disease. Wherever a tumor becomes ulcerated and infected the condition of the patient rapidly changes for the worse. For this reason a palliative operation designed to remove the septic area may produce marked benefit.

The gastric hydrochloric acid is diminished or absent in the majority of cases of cancer of the stomach. Cancer of other organs may also produce a diminution.

Acidosis may occur, with the appearance of diacetic acid and acetone in the urine. This is probably solely due to the protein loss and inanition.

EXPERIMENTAL TRANSPLANTATION OF TUMORS

After generations of histological study of tumors in man we have advanced little along the road to an understanding of their nature, and we turn expectantly to the experimental method as practiced upon animals. Both innocent and malignant tumors are found in mammals, birds, amphibia, and fishes, but the greater part of the work has been done upon the mouse for reasons of convenience.

It is possible to transplant a tumor occurring spontaneously in a mouse to other mice, and by continuing the transplantation to study the tumor over a period of many years under experimental conditions

which can be varied at will. It is at once evident what great advantages this method possesses over the study of tumors in human pathology.

When a tumor such as a breast carcinoma of a mouse is transplanted into a series of mice, it will die in a majority of the cases, but in 5 per cent the transplantation will take. After a series of transplantations, the tumor becomes so adapted that it will grow in almost every case. The fate of a successful graft is as follows. At the end of 24 hours a connective tissue reaction can be observed around the graft, the fibroblasts proliferate, and new capillaries are formed. At the same time the stroma of the graft begins to degenerate, and by the third day this degeneration is complete. The new granulation tissue invades the graft, vascularizes it, and by the end of the second week a completely new stroma is formed. The fate of the graft depends entirely on the formation of this new stroma. If this does not take place the graft will die. In an immune animal the new stroma is not supplied, in a susceptible animal it is. The new tumor is formed from parenchyma cells of the graft, and not at all from those of the host.

In some cases the new tumor after growing for some time may die. In such a case it is impossible to reinoculate the animal, which is now immune. Similar immunity can be produced by the inoculation of normal living tissue or of red blood corpuscles. The tissue, however, must be from the same species of animal. Rat tissue will not immunize a mouse. The immunity lasts for about 10 weeks. Unfortunately no one has ever succeeded in producing immunity to a growing tumor, nor can immunity be transferred passively to another animal.

Mice vary markedly in their susceptibility to inoculation, and it is possible by the aid of Mendelian principles to breed a strain of mice which is extremely susceptible and another which is equally immune. The work of Maud Slye is especially notable in this respect.

Until very recently all attempts to transplant a tumor from one animal to another of a different species have failed. Murphy has shown that this failure was due to the defensive action of the lymphocytes against the tumor graft. When the lymphoid tissue of an animal is injured by X-rays, the animal becomes much more susceptible to tumor transplantation from another animal of the same species.

In 1921 Shirai, followed by Murphy in 1922, succeeded in transplanting a tumor into the brain of an animal of another species. By selecting this site a mouse sarcoma was successfully grown in the brains of rats, guinea pigs, and pigeons. The brain, of course, is completely lacking in lymphoid tissue. Murphy made the additional interesting observation that when a piece of the animal's own spleen was inoculated into the brain along with the heteroplastic tumor tissue, the tumor failed to grow in every instance. This only occurred when the animal's own spleen was used. Should the graft come in contact with the ependyma lining the ventricle a cellular reaction occurs similar to that which takes place in subcutaneous tissues, and the graft fails to grow.

Several instances have been recorded by Ehrlich, Bashford, and others in which a tumor which was originally a typical carcinoma has become transformed into a sarcoma, which was then transmitted as such for many generations. In such cases the stroma has taken on sarcomatous characters, and has outgrown the original carcinoma. It has been possible to separate the two strains, and to continue them independently.

Perhaps the most remarkable tumor studied experimentally is the chicken sarcoma of Peyton Rous. This tumor can not only be transmitted with the greatest readiness by the inoculation of the tumor cells, but a cell-free extract obtained by passage through a Berkefeld filter reproduces a similar growth. It is of course possible that we are here dealing with an infective granuloma, which it is notoriously difficult to differentiate from a sarcoma, but the sections certainly show the appearance of an absolutely typical sarcoma.

Until quite recently experimental work on cancer was limited to the transference of a tumor naturally occurring in one animal to the tissues of another. It is now possible to produce at will in animals true tumors of their own tissues. Various experimental methods have been applied, such as the use of X-rays, animal parasites, paraffin, arsenic, and tar. Of these tar gives by far the best results. The tar tumor is identical in behavior and histological structure with the spontaneous tumor. The tar may be applied to the skin, or it may be injected into the mammary gland. As might be expected, the irritant has to be applied for a long period. In the mouse most of the tumors develop in from six to nine months, but the time may be as short as three and as long as eighteen months. The tar is applied to the skin every other day.

Animals with tar cancer cannot be inoculated again by a second tarring, nor can tar cancer be induced in an animal with a spontaneous cancer. Some profound systemic constitutional change evidently takes place in an animal in which cancer has developed, which renders it immune. If this change could only be detected by means of some immunological or other reaction it would solve the problem of the early diagnosis of malignant disease. The immunity appears to be different in character from that produced by tumor inoculation, for tar cancer can be produced in animals immunized by tumor inoculation, and tumors can be inoculated into tar immunes.

The recent work of Drew on the cultivation of tumors and tissues *in vitro* is of particular interest. Drew obtained pure cultures of a tissue such as kidney epithelium or kidney connective tissue by placing a minute globule of mercury over a separate clump of the desired cells, subjecting the tissue culture to the ultra-violet light of a mercury-vapor lamp, and then cultivating the tissue thus protected. The same method was employed for obtaining pure cultures of tumor cells. The kidney epithelium would grow in an undifferentiated sheet until the correct dose of connective tissue cells was added, when definite renal tubules were formed. The heart muscle cells pulsated, and

the mammary epithelium from a pregnant animal produced fat droplets which made the culture fluid quite milky.

Embryonic tissue and tumor tissue grow at once when placed in a suitable medium, but adult tissues show a curious lag of from ten to fourteen days. Drew found that when adult tissue such as rat kidney or liver was disintegrated by autolysis at 37° C. for two hours, the filtered extract when added to an adult tissue culture exercised such a stimulating effect that the lag was abolished and growth took place at once. This effect was not observed when the kidney or liver was kept at 0° C. for two hours instead of at 37° C., for autolysis was inhibited

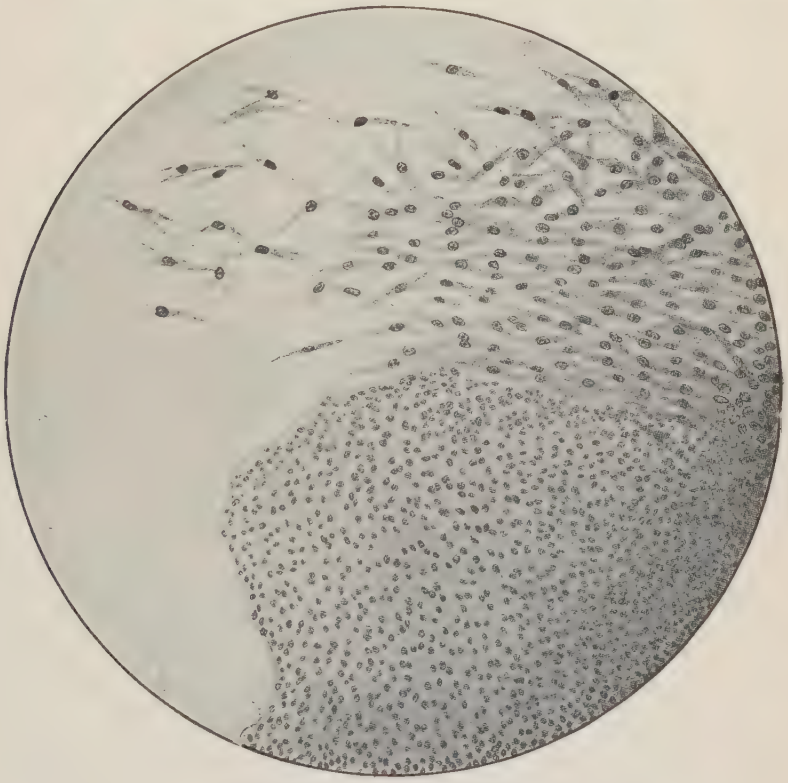


Fig. 31.—Epithelium and connective tissue growing side by side in a culture made from the intestine of an embryo. (MacCallum.)

and the stimulating substances were not produced. The stimulus appears to be analogous to that which damaged cells exert on cell proliferation in the process of repair. Drew further made the remarkably interesting observation that when tumor tissue such as a rapidly growing mouse carcinoma was employed for the production of this activation instead of normal adult tissue, a cold extract (at 0° C.) was even richer in stimulating substances than the normal autolysed tissue. Apparently some stimulant is produced spontaneously by the tumor cells,

even without the intervention of autolysis, which continues to act upon the surrounding cells so that the process becomes continuous and automatic.

THE EFFECT OF RADIATION ON CARCINOMA

In considering the effect of radiation, whether by X-rays or by radium, upon malignant tumors, we have to consider the effect (1) on the tissues, (2) on the tumor itself.

1. *Effect on the Tissues.*—The radiation acts as an irritant to the tissues and induces the production of an inflammatory exudate. Both serum and cells are poured out. The cells are polymorphonuclear leucocytes, which are replaced by lymphocytes and plasma cells. Eosinophils are often present in large numbers. They apparently play some important defensive rôle, for they are especially abundant in those cases which respond best to radiation. Indeed some observers have gone so far as to base a prognosis upon the presence or absence of eosinophilia in malignant tumors treated with radium. A fibroblastic reaction occurs later, the fibroblasts lay down collagen fibrils, and the final result is a dense fibrosis. The blood vessels show a marked reaction, and the local obliterative endarteritis which results greatly diminishes the blood supply to the part. Thrombosis is a common accompaniment.

2. *Effect on the Tumor.*—It has been said that very small doses act as a stimulant to the tumor cells. Whether this is so or not there can be no doubt that large doses produce marked degeneration in these cells. A necrobiosis of the cell occurs, with complete breaking up or chromatolysis of the nucleus, and granulation and vacuolation of the cytoplasm. Mitotic nuclei are particularly vulnerable, so that cells undergoing mitotic division and those rich in nuclear chromatin respond very readily. The radiation appears to exert a certain degree of selective action. The more immature and embryonic the cells the greater the effect produced. A basal-cell carcinoma (rodent ulcer) is much more radiosensitive than a squamous carcinoma (epithelioma). A highly cellular tumor with little connective tissue is much more sensitive than a comparatively non-cellular tumor with an abundant stroma. Perhaps the tumor which responds most readily to radiation is the lymphosarcoma, a highly cellular tumor, which sometimes fairly melts away under this method of treatment. Hodgkin's disease in the early stages, which are soft and cellular, may completely disappear under moderate radiation, whereas in the later stages, which are firm and fibrous, little effect may be produced.

Ewing has given a masterly analysis of the whole question in a recent Mütter Lecture. He gives the relative radiosensibility of tumors as follows:

1. Lymphoma; lymphocytoma, lymphosarcoma, myeloma.
2. Embryonal tumors; carcinoma of the testis and ovary, basal-cell carcinoma.

3. Cellular anaplastic adult tumors; "round-cell" carcinoma, diffuse carcinoma.

4. Desmoplastic tumors; carcinoma simplex, fibrocarcinoma, squamous carcinoma.

5. Adenocarcinoma; adenocarcinoma of the uterus, intestine, breast, etc.

6. Fibroblastic sarcoma, osteosarcoma, neurosarcoma.

Ewing points out that radiation may be made to act in other ways than that of producing autolytic degeneration of the tumor cells. When radium needles are inserted into a squamous carcinoma, which is notoriously resistant to external radiation, a caustic effect is produced which results in sloughing and destruction of the tumor. Lingual, buccal, and tonsillar cancer may yield in a satisfactory manner to this procedure. The method is widely employed in the treatment of carcinoma of the cervix of the uterus. If the needles are inserted into the infected lymph nodes still better results will be obtained. Another method of producing this caustic effect is by the interstitial injection of radioactive deposit in salt solution. The caustic action is produced by the alpha and beta rays.

There is still another effect of radiation therapy which must be distinguished. To quote from Ewing's paper: "It has long been observed that when one radiated certain deep-lying tumors of the more resistant class, such as adenocarcinoma of the corpus uteri or osteosarcoma of bone, the tumors failed to disappear, but their growth was inhibited and the tumors remained in a state of suspended growth with somewhat altered structure of a less malignant type. Under such treatment I have observed an osteosarcoma become converted into a solid, quiescent, highly osseous tumor. These observations indicate that radiation is capable of restraining the growth of tumor cells without causing either autolysis or necrosis, and of transforming functionless lawless cell growths into more organized and functioning tissues."

There are thus three main types of reaction to radiation which appear to be fundamentally different. These are:

1. *Autolytic degeneration,* observed mainly in the group of embryonal tumors.

2. *Caustic destruction,* employed in the treatment of resistant adult squamous carcinoma by bare radium emanation tubes.

3. *Growth restraint,* illustrated in the slow recession of resistant tumors under deep radiation.

The effect of radiation on the tumor cells is of great interest in relation to the production of immunity. Some tumors, such as Jensen's rat sarcoma, "take" in a large majority of the animals into which they are inoculated. If, however, the tumor graft be first given an accurately measured dose of X-rays or the gamma rays from radium it will no longer grow upon inoculation. By the end of three or four days after inoculation the tumor cells will be found to be

surrounded by lymphocytes, and in the course of ten days no trace of them can be found. When the inoculated animal is now re-inoculated with a piece of actively growing tumor it will be found to be immune.

To what extent these experimental results can be applied to man it is not at present possible to say. Attempts have already been made to treat human carcinoma by removing a piece of tumor, radiating it, and then re-inoculating it into the patient. It must be remembered, however, that it is one thing to produce immunity to a grafted tumor, but it is quite another thing to produce immunity to a tumor occurring spontaneously in an animal.

HEREDITY IN CANCER

The influence of heredity on the occurrence of malignant disease is a subject which has always aroused a great deal of interest. Many studies have been made on so-called "cancer families," and some of the instances recorded have certainly been remarkable. With these isolated instances, however, it is hard to get away from the suspicion that chance may be a factor of importance. The great difficulty has been to trace the lineage of the human cases far enough back, and to get reliable vital statistics based upon thorough post-mortem examination.

For these reasons resort has been had to breeding experiments on animals, and the results have thrown a flood of light on the relation of heredity to the occurrence of both carcinoma and sarcoma. These experiments are of two kinds, depending on whether they deal with transplanted or spontaneous tumors.

Transplanted Tumors.—Certain strains of the same species vary greatly in their susceptibility to transplanted tumors. Leo Loeb found that a tumor which occurred spontaneously in the Japanese waltzing mouse could be transferred successfully to 100 per cent of this kind of mouse, but not at all to ordinary laboratory mice. A tumor which would grow in nearly 100 per cent of Berlin mice would only take in 24 per cent of Hamburg mice, and not at all in Christiania mice.

Moreover heredity plays a definite part in the transmission of the susceptibility to inoculation. If Japanese waltzing mice are bred with ordinary mice the first generation of hybrids is susceptible to the inoculation of a tumor originating in a Japanese waltzing mouse, whilst the second and third generation made by breeding from the first generation are insusceptible. The characters of waltzing and susceptibility to cancer behave as Mendelian dominant and recessive unit characters, for the first generation are not waltzers but are susceptible, whilst the second and third generations are waltzers but are unsusceptible.

It must be realized, however, that a transplanted tumor is fundamentally different from a spontaneous tumor. A transplanted tumor, no matter through how many generations it has passed, is never composed of the cells of the animal in which it grows, but always of

the cells of the animal from which it was originally obtained. For this reason we turn to the behavior of spontaneous tumors in animals, which is much more analogous to the conditions prevailing in the human subject.

Spontaneous Tumors.—By far the most complete and important work in this field is that of Miss Maud Slye on the spontaneous tumors of mice. Miss Slye's work is of such interest in its bearing on human pathology that her main results, as recently summarized by Gideon Wells who examined the pathological material, will be given here.

Miss Slye has bred more than 40,000 mice under such careful conditions that they have been enabled to attain to their normal maximum age. Every one of the 40,000 have been submitted to post-mortem examination. All told, there have been at least 5,000 spontaneous tumors.

One of the first facts to emerge from this careful examination is that cancer in mice appears in most of the forms seen in man. Mammary cancer is by far the commonest growth, but in addition there were 160 primary tumors of the lung in the first 6,000 mice, 28 primary liver tumors in the first 10,000, 87 sarcomas in 12,000 mice, and many tumors of the testis, squamous cell carcinomas of the skin and mouth, basal cell carcinomas of the head, and ovarian carcinomas. In 33,000 mice there were 16 primary renal and 4 adrenal tumors.

The tendency to develop cancer and the capacity to resist it are unquestionably influenced by heredity, the resistance behaving like a typical Mendelian dominant character, whilst the susceptibility behaves like a recessive. When a cancer mouse derived from a cancer strain is crossed with a cancer-free mouse derived from a cancer-free strain the first generation of hybrids never show cancer, susceptibility to cancer being a recessive character. The second generation of hybrids derived from the first will develop cancer in strict Mendelian proportions. As Miss Slye remarks, cancer and non-cancer tendencies being unit characters, it is possible to manipulate them by selective breeding, and thus implant them indelibly in or eliminate them permanently and completely from any species. Even the site and character of the tumor is governed by the same considerations, for one strain of mice was developed which yielded over a hundred primary carcinomas of the liver, although in all the other mice examined not a single liver tumor was found.

These remarkable results cannot of course be applied wholesale to man, as we cannot hope even to approach the principle of selective breeding possible in an animal experiment, but evidence has already accumulated to indicate that in human cancer resistance behaves as a dominant and susceptibility as a recessive character and that these characters can be transmitted. Certain rare tumors such as glioma of the eye, neurofibromatosis, and multiple cartilaginous exostoses show a family occurrence. Newton reports a family of 16 children 10 of whom died of retinal glioma, in seven of which the disease was bilateral. In another family 8 children were similarly affected.

Instances of cancer families are to be found in the literature. The most famous example is one reported by Broca in 1866; of 26 members of this family, mother, children, and grandchildren, reaching the age of thirty, 16 died of cancer of the breast, liver, or uterus. Warthin cites a family in which, of 48 descendants of a cancerous grandfather, 17 suffered from cancer, and many of the survivors were still below the usual cancer age. If one parent suffers from cancer it will not of course follow that the offspring are cancerous, for the other parent may be resistant, and resistance is the dominant character. If both parents are cancerous one might expect to find a marked incidence in the children, although many of these may die of other diseases before they reach the cancer age. In one of Warthin's instances a cancerous father and a cancerous mother had six children; all died of cancer, as did the only grandchild; thus the entire family of nine members in three generations all died of cancer.

From the foregoing we may say that a tendency towards cancer can be transmitted from parent to offspring certainly in the case of animals and possibly or indeed probably in the case of man. This tendency is a predisposing factor. The exciting factor which initiates the abnormal cell proliferation has still to be discovered. An interesting illustration of this in another field was given recently by Hagedoorn-La Brand. A colony of mice composed of Japanese mice, large albinos, and hybrids of these two was attacked by an epidemic of staphylococcus infection, which killed all the Japanese mice but none of the albinos. In the first hybrid generation none died, the resistance of the albinos being a dominant character. In the second hybrid generation, of 125 animals 91 lived and 34 died; according to Mendelian principles the number would have been 93 and 31.

Spontaneous Cure in Carcinoma.—From what has already been said in this chapter it will be evident that in a study of the natural history of a malignant growth two factors may be detected; there is the destructive and anarchistic tendency of the tumor cells, but there is also the restraining influence of the tissues, an influence of which the outward signs are lymphocytic infiltration, eosinophilia, and fibrosis. As a rule this attempt on the part of the tissues is of no avail so far as the life of the patient is concerned, but histological evidence may often be found, for instance in carcinoma of the breast, that groups of tumor cells have been strangled or encapsulated by fibrous tissue.

In exceptional cases secondary nodules may disappear for no apparent reason. This is again exemplified by carcinoma of the breast. Pearce Gould records a remarkable case in which the patient presented very numerous secondary skin nodules, enlarged axillary glands, and a cancerous fracture of the neck of the femur. The nodules disappeared, the glands returned to normal size, and the fracture united. I have reported an equally strange case. The patient was under the care of Dr. J. E. Lehmann. A scirrhous carcinoma of the right breast (diagnosed microscopically) was removed towards the end of 1915. Early next year she returned with unmistakable metastatic involve-

ment of the right humerus. Six months later the X-ray picture showed metastases in the right humerus, the right femur, and the pelvis. She was not seen again until October, 1917, when she was admitted to the Winnipeg General Hospital bed-ridden, unable to feed herself, and with spontaneous fractures of both upper arms. Over the vault of the skull numerous firm nodules could be felt. X-ray studies showed an astonishing involvement of the skeleton. It almost appeared as if not a bone in the body had been spared. There were widespread metastases in the skull, humerus, radius, ulna, femur, tibia, and fibula on both sides, the pelvis, and the small bones of the hands and feet. During the next four months, while the patient was waiting to be admitted to a home for incurables, the clinical picture underwent a remarkable transformation. The nodules in the head disappeared, the fractures of the arms united, strength returned to the legs, she was able to sit up and knit, and when she left the hospital she could walk without assistance. About six months later she succumbed to metastases in the internal organs. This is the usual outcome in such cases.

Removal of the primary growth is sometimes followed by disappearance of the metastases. This is particularly true for primary carcinoma of the ovary. The secondary growths in chorionepithelioma may disappear either spontaneously or after removal of the uterine tumor. In rare but undoubted cases an entire carcinoma, primary growth as well as metastases, has undergone spontaneous cure.

CLASSIFICATION OF TUMORS

It is safe to say that there is at present no satisfactory classification of tumors. Nor, indeed, is such a classification possible with our present knowledge, for we are completely ignorant as to the nature and the cause of new growth. The classification which will be used here is merely a working classification based on the type of tissue from which the tumor originates, but as in many cases it is difficult or impossible to say what that tissue is, the method is far from ideal.

Tumors for our present purpose may be arranged as follows:

1. Connective tissue tumors.
   - A. Innocent
     - Fibroma.
     - Lipoma.
     - Myxoma.
     - Chondroma.
     - Osteoma.
   - B. Malignant — Sarcoma.
2. Muscle tissue tumors
   - Leiomyoma.
   - Rhabdomyoma.
3. Epithelial tumors.
   - A. Innocent
     - Papilloma.
     - Adenoma.
   - B. Malignant — Carcinoma.

4. Nervous tissue tumors.	Glioma
5. Endothelial tissue tumor	Endothelioma. Hemangioma. Lymphangioma.
6. Pigmented tumors	Nevus. Melanoma.
7. Adrenal tissue tumors	Hypernephroma.
8. Chorionepithelioma.	
9. Teratomata.	

FIBROMA

A fibroma is a tumor composed of fibrous tissue. It consists of fibroblasts with a varying amount of intervening fibers. It varies greatly in consistency, and two types are commonly described, the hard and the soft, but all intermediate grades may be met with. Considering the wide distribution of fibrous tissue it is somewhat remarkable that fibromata are not common. As a matter of fact a pure fibroma is a very rare tumor.

The *hard* fibroma is globular in outline, but may be lobulated. It is easily separated from the tissue from which it arises. When cut there is a peculiar creaking sensation as of cartilage. The cut surface is flat or slightly convex, white in color, and intersected by glistening bands.

Microscopically it consists of bundles of white fibers cut in different planes, between which are small elongated nuclei representing the flattened connective tissue cells. The vessels are small and few in number, but may be large and thin-walled. In the latter case they may be unable to collapse, so that there may be free hemorrhage when the tumor is cut into.

The *soft* fibroma displays no glistening surface. It consists of loose areolar tissue, the slender bundles of which form an open network sometimes containing abundant fluid.

Fibromata may occur in almost any part of the body, but the usual sites are the skin, mucous membranes, muscles, bone, nerves, and certain of the viscera.

Skin.—A fibroma may occur as a hard nodule in the skin or subcutaneous tissue. Soft fibromas, often pedunculated, are called molluscum fibrosum, but are really tumors of cutaneous nerves.

Keloid or cheloid is not a true tumor, but a tumor-like condition which generally originates in a scar. It is a firm, smooth, raised patch from which extend claw-like processes, and it may come to cover a considerable area. Some persons have an idiosyncrasy to the development of keloid, and it is common in negroes. It consists of very dense fibrous tissue, the bundles of which run parallel with the surface.

Mucous Membranes.—The fibroma arises in the submucous coat, and often becomes pedunculated. It occurs in the esophagus, stomach, and intestines. In the latter position it may cause intussusception.

Muscles.—The commonest site is the sheath of the rectus. The growth arises from the fascia. Tumors in this position are more often

fibro-sarcomas, and are sometimes called desmoid tumors from their bundle-like structure.

Bone.—Fibromas of bone are rare, and frequently prove to be fibro-sarcomas. A fibrous polypus may grow from the naso-pharynx, and extend into the Eustachian tube or the orbit. A fibrous tumor growing from the alveolus of the jaw is called a fibrous epulis, and must be distinguished from the giant-celled epulis to be described later.

Nerves.—It is somewhat curious that one of the important sites of fibrous tumors is the nerves. Neurofibromata may be single or

FIG. 32.—Multiple neurofibromata of the peripheral nerves. *A*, Nerves of the right arm; *B*, the left sciatic with its branches; *C*, the left anterior crural with its branches. (Prudden's case, from Ewing's Neoplastic Diseases.)

multiple, and the two classes present marked differences. The *single* fibroma may occur as a hard isolated tumor on one of the large nerve trunks growing from the epineurium; it is neither painful nor tender. Or it may be attached to a cutaneous nerve, in which case it is often exquisitely tender, and is called a "painful subcutaneous tubercle." A common position for such a nodule is the upper part of the thigh.

Multiple fibromata may occur as separate tumors on the nerves, usually the cutaneous branches, giving rise to soft nodules in the skin, often several hundred in number, distributed over the whole body, and called *molluscum fibrosum*, a condition also known as Von Recklinghausen's disease. The skin may be pigmented in patches, or there may be groups of brown spots, like freckles. One case which I studied resembled Addison's disease. These neurofibromata not infrequently develop sarcomatous characters. Or a diffuse neurofibromatosis may occur in which there is a diffuse overgrowth of the endoneurium causing separation of the nerve fibers and giving rise to a *plexiform neuroma*. This condition most commonly occurs in the head and neck, especially in the distribution of the fifth cranial and upper cervical nerves. In the orbit it produces marked exophthalmos. Rarely it occurs in the tongue, giving rise to one form of macroglossia.

Visceral—A pure fibroma is occasionally found in the ovary as a hard mass which may attain a considerable size. In the kidney there may be small, hard, fibrous nodules in the cortex or the medulla.

Fibrous tissue is often a prominent feature in adenomata of the breast and myomata of the uterus, but it does not form an essential part of the new growth, although it may modify its character very considerably.

Xanthoma.—This is a tumor of a peculiar golden-yellow color which in over 90 per cent of the cases is situated in the eyelids. Occasionally it occurs in multiple form in other regions, and, as in the case of multiple neuro-fibromata, it may follow the distribution of the cutaneous nerves. Similar growths are found in the serous membranes, in the tendon sheaths, and in the pancreas in diabetes. The generalized form may be associated with jaundice or with diabetes (xanthoma diabeticorum).

The tumor, which appears to be a form of fibroma, consists of large swollen polyhedral cells and smaller spindle-shaped cells. These cells are filled with globules of yellow lipoid material similar to that which occurs in the adrenal cortex, the corpus luteum of the ovary, and the "strawberry gall bladder." It is an ester of cholesterol.

LIPOMA

A lipoma consists of normal fat arranged usually but not always in irregular lobules separated by fibrous septa. It is surrounded by a delicate capsule of connective tissue, and is very readily shelled out. It may grow to any size, and often becomes pedunculated. It is the most innocent example of tumor growth known, and there is no malignant form. Like a true tumor, however, it is outside the pale of the body laws, and refuses to part with its fat in general wasting diseases.

The common site is the subcutaneous tissue, especially of the neck, shoulders, back, and buttocks. It may occur in the mesenteric and

retroperitoneal fat, and rarely in the submucous coat of the stomach and intestines.

The so-called "diffuse lipoma," generally met with in the neck, is not a true tumor. It merges with the surrounding fat.

A lipoma can be diagnosed from the following characters. It forms a soft, painless, usually lobulated mass, the overlying skin being often slightly dimpled owing to fibrous bands passing from it down between the lobules. It moves readily over the deep fascia, and can be distinguished from a collection of fluid in that it possesses a very definite margin which can be felt through the skin.

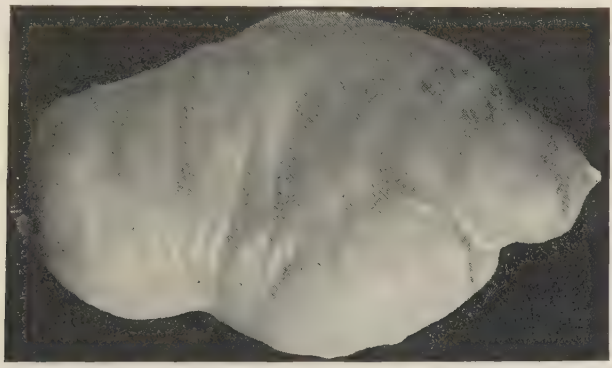


FIG. 33.—Lipoma. The encapsulated character of this growth is well shown.

MYXOMA

A true myxoma is one of the rarest of tumors. On the other hand mucoid degeneration is of common occurrence in many connective tissue tumors such as fibromas, chondromas and sarcomas. The mucous polypus of the nose bears no relation to a myxoma. Indeed it is not a neoplasm at all, but a mass of edematous inflammatory tissue, jelly-like in consistence, and containing mast cells and eosinophils.

Microscopically a myxoma resembles Wharton's jelly or the vitreous humor of the eye in structure. It consists of a delicate reticulum of branched connective tissue cells, in the meshes of which there is an abundant mucinous fluid, which becomes granular on the addition of acetic acid, and can be stained differentially with muci-carmine.

A myxoma occurs in the same positions as fibromata. It is perfectly encapsulated and is readily shelled out. A tumor diagnosed as a myxoma on removal not infrequently proves later to be a sarcoma.

CHONDROMA

A chondroma is a tumor consisting of cartilage, firm in consistence, bluish-grey in color, and with a somewhat translucent surface. When growing to any size it is usually lobulated, and possesses a well-marked capsule, so that it can be readily shelled out.

Microscopically it presents the appearance of normal cartilage, but the cells do not as a rule have so regular an arrangement.

It grows in connection with bones, and is also met with in mixed tumors of glands, usually malignant in character.

Containing practically no vessels and deriving its nourishment only from the vessels in the capsule, it is peculiarly liable to myxomatous and calcareous degeneration in the central parts.

The parts chiefly affected are the ends of the diaphysis of the long bones, especially in young people, where ossification is common, the metacarpals and phalanges of the hand, often multiple, where ossification is rare, and the bones of the thorax and pelvis, where they may attain a large size and cause serious obstruction of the cavity.

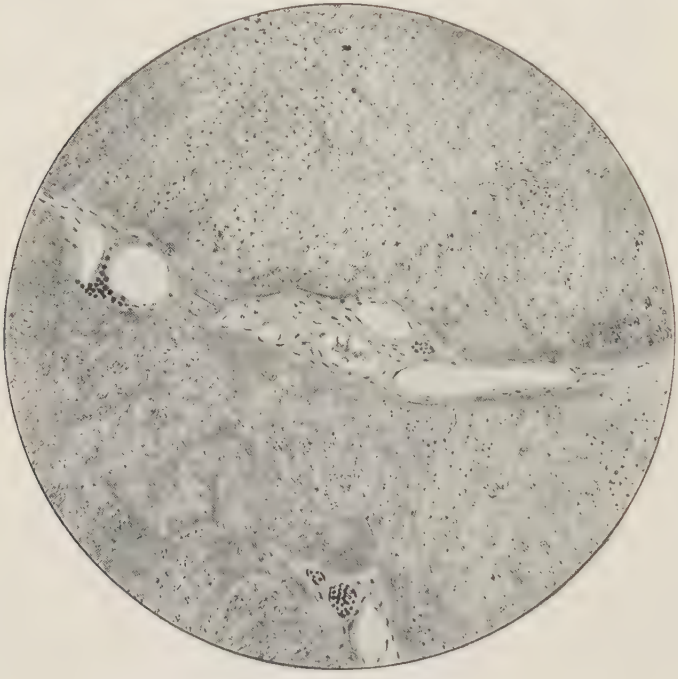


FIG. 34.—Chondroma.

Mixed tumors of the testicle, the parotid and submaxillary glands, and rarely the breast, may contain such a large proportion of cartilage as to present the appearance of a pure chondroma.

OSTEOMA

A true osteoma is a somewhat rare tumor. New formations of bone are of common occurrence, for example the callus at the site of a fracture, the masses of bone which may be formed in a muscle as the result of injury, the formations around joints the seat of chronic arthritis, etc. These, however, are not examples of tumor growth.

As bone consists of two varieties, the cancellous and the compact, so also may osteomas be similarly divided.

The *cancellous osteoma* occurs in young growing subjects at the end of the diaphysis close to the epiphyseal line, although with the growth of the bone the distance from that line may become greater. It almost certainly originates as a piece of the epiphyseal cartilage which has become separated and then ossified. It is usually pedunculated, and covered at the growing tip by a cap of cartilage. Unless this cartilage is removed when the tumor is operated on it will recur. The usual site is the lower end of the femur or the upper end of the tibia.

The *subungual exostosis* is a variety of cancellous osteoma which grows from the dorsum of the distal phalanx of the big toe. It causes intense pain through raising the nail, finally causing it to break away.

The *compact osteoma*, often called an ivory exostosis, is an extremely hard sessile tumor usually growing from the vault of the skull. It occasionally originates in the frontal or ethmoidal sinuses, from which it may invade the orbit.

SARCOMA

A sarcoma is a malignant tumor of connective tissue. The group as at present constituted is large, indefinite, and includes various members which have no rightful place there. Malignant tumors of muscle, lymphoid tissue, and pigment cells should be excluded, and the term strictly confined to tumors of connective tissue origin. This, however, is at present a counsel of perfection, for such a term as lympho-sarcoma is so deeply rooted in the literature that it cannot easily be eradicated.

The histological diagnosis of sarcoma may be one of the most difficult tasks in pathology. A typical sarcoma can be recognized at a glance, but there are numberless gradations towards the innocent connective tissue growths which may make differentiation very hard. To complicate the problem still further simple inflammatory tissue, especially when undergoing repair, may bear so close a resemblance to certain forms of sarcoma as to deceive the very elect.

Sarcomas may be divided into two large groups. In one, the cells are embryonic in type, and there is so little differentiation towards the adult type of tissue that it is impossible to say from which tissue the tumor has originated. Such growths, as might be expected, are of a most malignant type, and are named according to the appearance which the cell presents, as small round-celled sarcoma, large round-celled sarcoma, mixed-celled sarcoma, etc. In the other, differentiation has proceeded far enough for the tissue to be recognized, and we have a fibro-sarcoma, myxo-sarcoma, chondro-sarcoma, and osteo-sarcoma. These growths are less malignant than those of the previous group.

Degeneration is peculiarly liable to occur in a sarcoma, largely on account of the great rapidity of growth, which may outstrip the supply of nourishment. Hemorrhage is of such frequent occurrence, owing to the thin-walled character of the vessels, that its presence in a tumor should arouse suspicion of a sarcoma. It is attended by lique-

faction of the tissue, and a spurious cyst is formed containing bloody fluid. Mucoid degeneration is common, and the tumor may be mistaken for a myxoma. Fatty degeneration and calcification may occur, and part of a tumor growing from bone may become ossified—the ossifying sarcoma.

Malignancy.—In the group of sarcomas are included some of the most malignant tumors which attack the body. On the other hand there are some which can with difficulty be distinguished from innocent fibrous tissue growths. Recurrent fibroid used to be a common diagnosis for tumors which when first removed appeared quite innocent, but which recurred again and again, and with each removal showed a more definite histological appearance of malignancy. Speaking generally, the less the differentiation the greater is the malignancy, so that the small round-celled sarcoma has the doubtful honor of heading the list. The malignancy is evidenced in two ways, (1) by invasion, and (2) by the formation of metastases.

(1) The infiltrating powers of a sarcoma are notorious. A sarcoma of bone may infiltrate the surrounding muscles. A sarcoma of the maxilla may creep through all the foramina opening into the sphenomaxillary fossa and appear in the cranial cavity A sarcoma of the kidney may invade the renal vein and climb far up along the vena cava. On the other hand it is remarkable how slender a barrier may stop the spread of the tumor. One of the best examples of this is afforded by a sarcoma of bone in the neighborhood of a joint, where the articular cartilage usually effectively prevents the invasion of the joint. The explanation probably lies in the absence of vessels in the cartilage.

(2) Metastases are both early and widespread. The tumor spreads by the blood stream, gaining ready access to the veins on account of the thin-walled nature of its vessels. As would be expected, secondary growths are commonest in the lungs, and in the liver in sarcoma of organs drained by the portal circulation, but the distribution may be more widespread. Spread by the lymphatics is much less common, but secondary growths may be found in the lymph glands.

Naked-eye Appearance.—No general description is possible which will embrace all the varieties of sarcoma. Certain characters, however, would lead the observer to suspect the sarcomatous nature of the growth. A typical sarcoma, such as the round-celled variety, is soft in consistence, often closely resembling the white matter of the brain, of a greyish or pinkish white color, and presents a homogeneous appearance very different from the whorls of a fibroma or the cellular masses of a carcinoma. A spindle-celled sarcoma, such as that growing from the periosteum, may, however, have a distinctly striated appearance. Hemorrhage is frequent, as also are areas of softening and degeneration. The vessels supplying the tumor are usually large, although those in the stroma may be mere capillaries, so that alarming hemorrhage may occur if the tumor is incised during removal. There is no capsule.

Microscopic Appearance.—The tumor is highly cellular, and the stroma may be so scanty as to be almost invisible. The cells of a carcinoma are arranged in groups separated by a stroma usually abundant, but the stroma does not penetrate between the individual cells of a group, nor do the blood vessels. In these respects the tumor resembles the epithelium from which it arises. In a sarcoma, on the other hand, the cells are scattered uniformly throughout the tissue, and separated from one another by a delicate stroma in which run numerous thin-walled blood vessels. It is true that in the so-called alveolar sarcoma there is an attempted alveolar grouping of the cells in places, but in other parts the above description will be found to hold. In the more rapidly growing forms mitotic figures are numerous, and in all doubtful cases these should be carefully searched for. It must be remembered that in actively growing granulation tissue the fibro-

FIG. 35.—Round-cell sarcoma. The thin-walled vessels are lined by a single layer of endothelium.

blasts may show occasional mitosis. The walls of the blood vessels are characteristically thin, and in many cases appear to be formed of little more than the cells of the tumor. It is easy to understand, therefore, the frequency both of hemorrhage and invasion of the blood stream.

Sites.—Connective tissue is found in every part of the body, and the distribution of sarcomata is correspondingly wide. They are specially common, however, in bone, periosteum, fascia, and muscle,

where they are liable to be confused with gummata, and in the ovary and the testicle.

Round-cell Sarcoma.—This is the most malignant variety of sarcoma. The cells, which may be small or large, are separated by an extremely scanty stroma, and the vessels are numerous and poorly developed. In the small-cell variety the nucleus is relatively large and dense, and the cytoplasm scanty, so that the cell closely resembles an ordinary lymphocyte. In the large-cell form the nucleus is more vesicular and stains less darkly, the cytoplasm is more abundant, and the stroma may be better marked.

Spindle-cell Sarcoma.—The cells which are elongated or spindle-shaped may be small, large, or oat-like. They are frequently arranged

Fig. 36.—Spindle-cell sarcoma. The elongated cells are arranged in bundles and whorls.

in bundles, an arrangement which may give the cut surface a striated appearance to the naked eye. The invasive characters are less marked, and metastases are not set up at so early a date as in the round-celled variety.

Giant-cell Sarcoma.—*Giant-cell Tumor.*—The nomenclature of this well-defined group of neoplasms has in the past been the cause of a considerable amount of confusion. A tumor growing usually from the interior of the upper end of the tibia or the lower end of the femur has long been described, especially by English writers, as a myeloid

sarcoma, and as doubt has been cast upon its malignancy, it is now called a myeloma. Its most characteristic histological feature is the presence of numerous multinucleated giant-cells, and as similar cells are present in a form of epulis, or tumor of the mandible, the latter has also been classed as a myeloma. Finally, the term myeloma or multiple myelomata is applied to an entirely different condition in which multiple growths appear simultaneously in the bone marrow of the vertebræ, ribs, and cranium, accompanied by the appearance of a peculiar form of albumose in the urine.

The last named is the only condition which deserves the designation myeloma, and it will be considered subsequently. The giant-cell tumors growing from the ends of the long bones and from the lower

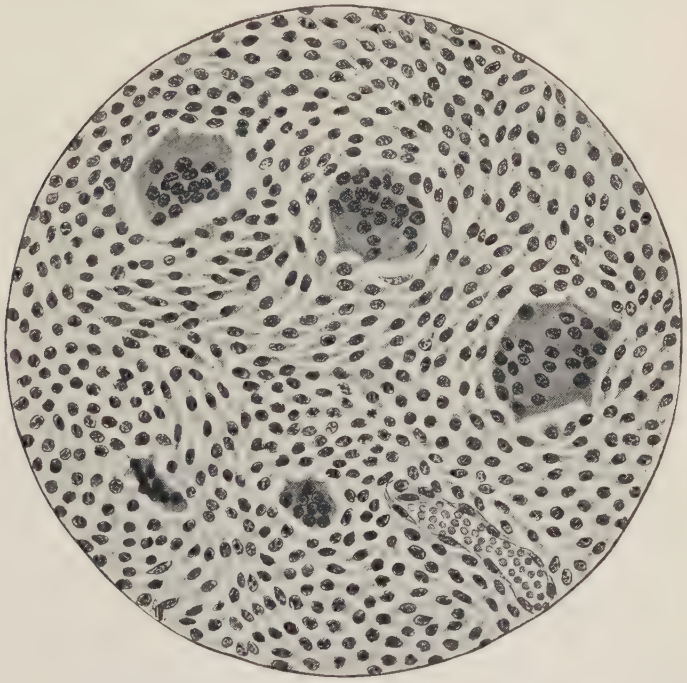


Fig. 37.—Giant-cell tumor, showing several large multinucleated cells of the foreign-body type.

jaw are not bone marrow tumors, but connective tissue growths arising from the periosteum or the endosteum. The giant cells are possibly foreign-body giant cells, called into being through the eroding action of the tumor—on bone. For the present they will be called giant-cell tumors. The tumor, although locally destructive, does not involve lymphatic glands, it does not recur when removed locally, and it never sets up distant metastases. The tumor occurs most frequently in adolescents and young adults.

Microscopically the tumor consists of a groundwork of small oval cells, sarcomatous in appearance, amongst which are scattered some-

what irregularly the characteristic giant cells. The latter are large, dark, multinucleated cells, the nuclei of which are as a rule situated centrally, in distinction to those of the giant cell of tuberculosis (Langhans' type) in which they are congregated at one end of an elliptical cell, or arranged round the periphery.

The form occurring in the neighborhood of the knee joint commences in the interior of the bone, which becomes expanded with the increasing growth until a mere egg-shell of bone is left. These tumors are extremely vascular, of a dark red or maroon color, and degeneration is common with the formation of cysts into which hemorrhage is very liable to occur. The mass is very soft and may be distinctly pulsatile. Local removal when possible is all that is required.

In the form growing from the jaw the gross characters are different. The tumor is firm, not unduly vascular, and commences in the periosteum, gradually eroding the bone from without. I have seen a growth of identical histological structure arising from the tendon sheath of the index finger.

Giant cells are not infrequent in ordinary sarcomas, especially those of the mixed-celled variety, but the appearance of such growths is very different from that of the tumor which has just been described.

The *fibro-sarcoma, chondro-sarcoma, and osteo-sarcoma* approach more closely to the innocent tumors of these tissues. In places there may be well formed cartilage or bone, in others the structure is more anaplastic, and the cells resemble those of a typical sarcoma. It is therefore well to examine more than one part of the growth. The progress of the condition is usually slow, and metastases are only set up at a late date.

Lymphosarcoma.—Although not arising from connective tissue, and thus not strictly to be included in the group of sarcomata, the lymphosarcoma may conveniently be considered here. It is a malignant tumor of lymphoid tissue, but although that tissue is of such wide distribution the lymphosarcomas are almost confined to three regions: the mediastinum, the cervical lymphatic glands, and the intestinal mucosa in the region of the cecum.

The chief characteristic of the tumor is that it spreads from one gland to another, creeping along a chain, until a large mass is formed, the separate members of which are matted together. At the same time it invades the surrounding structures, but it seldom gives rise to distant metastases, unless, it may be, in the lymphatic glands. Wide removal, if possible, is therefore often effective.

Microscopically it closely resembles in structure normal lymphoid tissue or a round-celled sarcoma. From the former, however, it differs in showing no trace of the architecture characteristic of a lymphatic gland, from the latter in possessing a delicate but very definite stroma such as is seldom seen in a round-celled sarcoma.

In the thorax it constitutes the commonest variety of "mediastinal tumor," surrounds the bronchi and the great vessels producing symptoms of obstruction, and may be diagnosed by the physical

signs and the X-ray picture. The lungs are often extensively invaded.

In the neck it has to be distinguished from other forms of lymphatic enlargement such as tuberculosis, Hodgkin's disease, and secondary carcinomatous growths.

In the cecum it may extend for some distance along the wall of the gut, involving the adjoining lymph glands, but without producing ulceration. Removal is possible if the disease has not progressed too far.

Melanotic Sarcoma.—This is not a connective tissue tumor, and will be considered elsewhere (page 211).

Muscle Tissue Tumors

Corresponding to the two kinds of muscle, plain and striated, there are two varieties of tumors, leiomyoma and rhabdomyoma; the former is very common, the latter very rare.

LEIOMYOMA

Plain muscle tumors may occur wherever plain muscle is found, and small nodules are not uncommon under the capsule of the kidney, and in the wall of the intestine where they may form polypoid growths which hang into the lumen of the bowel. In these positions they hardly ever produce symptoms and are of no practical importance.

In the uterus, on the other hand, they are extremely common, and may produce symptoms of great gravity. The tumor begins in the muscular wall, and may grow outwards becoming subperitoneal, or inwards becoming submucous. They are usually multiple and may be very numerous. A true myoma, the tumor may yet contain so large an amount of fibrous tissue as to justify the name fibro-myoma or the clinical term "fibroid." The fibrous tissue determines to a large extent the character of the tumor.

Naked Eye Appearance.—The tumor may vary from the size of a pea to that of a cocoanut. It is well encapsulated and easily enucleated. The consistence depends on the amount of fibrous tissue, but is usually firm and hard. On the cut surface bands or whorls of white fibers can be distinguished, intermingled with which is the yellowish or grey muscular tissue. So abundant may be the fibrous tissue that the tumor closely resembles a fibroma. Degenerative changes are frequent, altering the naked-eye appearance. One of the commonest of these is mucoid degeneration of the connective tissue, causing softening of the tumor and occasionally giving rise to cysts. Areas of necrosis may occur from deficient blood supply, followed later by calcification. "Red degeneration" of a fibroid is a condition in which the whole mass becomes dark red or cyanotic, and is probably a result of thrombosis of the veins. It is often associated with pregnancy.

Microscopically the fibroid consists of interlacing bundles of plain muscle fibers, separated by a varying amount of connective tissue. The muscular may be distinguished from the fibrous tissue by

observing that the nuclei of the former are plump, long, and blunt-pointed, whilst those of the latter are narrow, short, and pointed at the ends. Van Gieson's picro-fuchsin stain colors the muscle yellow and the fibrous tissue red.

The myoma is an innocent tumor, but occasionally it may take on malignant characters. The muscle fibers and their nuclei become swollen and flabby, mitotic figures are present, and the appearance is that of an actively growing tissue. Such a condition is often termed

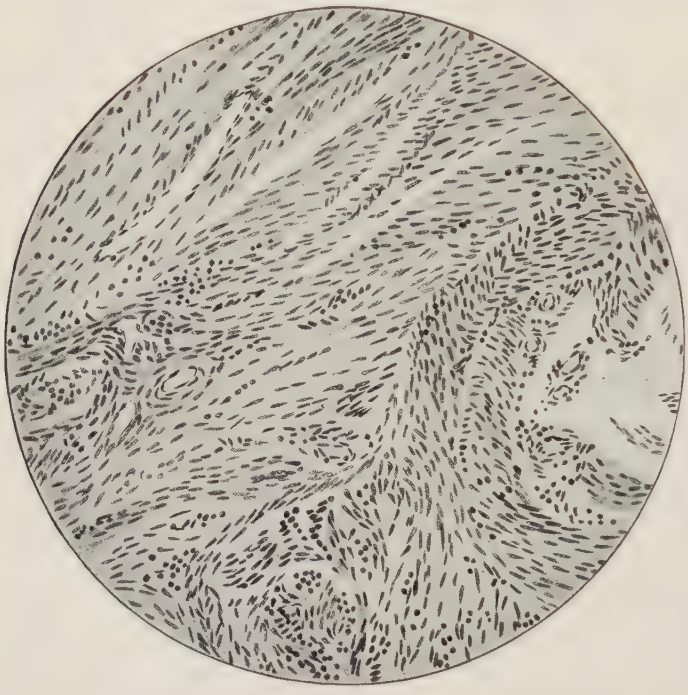


FIG. 38.—Myoma of uterus. The muscle cells are grouped into very definite bundles.

a myo-sarcoma. It should rather be called a malignant myoma, the term sarcoma being reserved for tumors of connective tissue origin.

RHABDOMYOMA

Tumors consisting of striated muscle are not only very rare, but they do not occur in voluntary muscle. They are found in the heart, kidney, testicle, and vagina. They are common in children, and probably arise from embryonic rudiments. As a rule they are malignant, but may occasionally be innocent.

EPITHELIAL TUMORS

Epithelium is a tissue which varies greatly in structure with its position in the body and the function it is destined to perform. It occurs in three main forms.

1. Squamous epithelium covering the skin, lips, mouth, tongue, pharynx, larynx, esophagus, vagina, and in a modified form the bladder.

2. Columnar epithelium lining the mucous membrane of the stomach, intestine, and uterus, and the tubular glands arising from that mucous membrane.

3. Epithelium, cubical or spheroidal in type, lining such acinous glands as the breast, pancreas, or prostate, or arranged in solid strands in organs like the liver.

In whatever form it occurs it presents certain common features. (1) The cells of which it is composed lie in apposition with one another, (2) they are arranged in groups, (3) the groups are separated by a fibrous stroma and (4) unlike the connective tissues the stroma does not intervene between the individual epithelial cells. Tumors arising from epithelium, however diverse in appearance, maintain these basal characteristics.

The innocent epithelial tumors reproduce the structure from which they originate; they are histioid in type. The malignant tumors may make no attempt to do so, or the attempt if made is never successful.

The innocent variety may assume two forms, the papilloma and the adenoma; the former arises from a surface, the latter from a gland.

PAPILLOMA

There are three varieties of papilloma which may conveniently be considered separately, depending on whether they arise from a squamous surface, from a mucous membrane, or from the wall of a cyst.

The squamous papilloma is commonest on the skin, but may occur in the larynx and other parts covered with stratified epithelium. It consists of branched processes covered by proliferated squamous epithelium, or there may be only a single massive process. On the skin it forms a wart. With each advance of knowledge, however, it becomes apparent that many of these papillomata are not true tumors, but merely the result of some unrecognized irritant. The cutaneous warts of children, which often come out in crops and disappear after a varying interval, are certainly infectious in nature. The venereal warts (condyloma acuminatum) occurring in the region of the genital organs are of a similar character. Some so-called warts are in reality pigmented tumors, and probably not epithelial in nature.

The mucous papilloma grows from a mucous membrane, generally that of the bladder and rectum, but it may occur in any part of the alimentary canal. It is a soft villous tumor growing from a slender stalk, and in the bladder the processes may be so numerous as to resemble seaweed. These tumors of the bladder are very liable to develop a malignant tendency. Many of them may be malignant from the beginning (see page 449). Infection with the Bilharzia may give rise to tumor-like masses in the bladder and rectum indistinguishable from a mucous papilloma, and these growths also may sometimes become malignant.

FIG. 39.—Squamous papilloma of skin.

FIG. 40.—Mucous papilloma of bladder.

The intracystic papilloma may resemble a wart or a mucous papilloma. The former is seen in the interior of cysts of the breast (Fig. 41), the latter in the ovarian cyst adenoma.

Fig. 41.—Breast. Duct papilloma.

ADENOMA

An adenoma is an innocent epithelial tumor of glandular origin. It varies in structure with the particular gland from which it arises. In an acinous gland such as the breast or kidney the cells surround acini in a perfectly regular manner, and may reproduce the glandular structure to perfection, even going so far as to produce the normal secretion of the organ. The lining cells are one or two layers in depth, but even when a number of layers are present this does not indicate malignancy. They rest upon a basement membrane formed of compressed connective tissue, and show no tendency to invade the surrounding tissue.

When the glandular secretion is abundant the acini of the tumor may become distended with fluid to form cysts, for they are not provided with ducts by means of which the secretion may escape. This is seen to best advantage in the ovary, where the acini are lined by tall columnar mucin-secreting cells, derived from a downgrowth of the superficial germinal epithelium, so that the tumor is called a cystadenoma, but it is also fairly common in the breast. The cells lining such cysts may atrophy from the pressure, becoming cubical or flattened, or they may proliferate and project as papillomata into the cyst spaces—a papillary cyst-adenoma.

Adenomata of the *breast* are of special importance on account of the difficulty sometimes experienced in distinguishing them clinically from carcinoma. They seldom occur as pure epithelial tumors, for there is usually a proliferation of fibrous tissue, more or less marked, the tumor being a fibro-adenoma. In many cases the fibrous overgrowth appears to be the dominant feature, that of the glandular tissue being secondary, so that the term adenofibroma would be more appropriate. The tumors present two varieties, one in which the fibrous tissue surrounds the gland spaces, the other in which it projects into the spaces. These pericanalicular and intracanalicular forms will be discussed more fully in the chapter dealing with diseases of the breast.

Adenomata of the *stomach* and *intestine* often project into the lumen, hanging by a slender stalk so as to form soft polypoid tumors which may give rise to intussusception.

In the *thyroid*, adenomata are very common, forming one variety of goiter. They may present the normal structure of the thyroid, except that the acini may be dilated and cystic, or they may be composed of small acini lined by large cuboidal cells and separated by an abundant stroma, thus resembling in structure the fetal or infantile thyroid, and called on that account fetal adenomata.

Adenomata of solid glandular organs such as the *liver* and *adrenal* consist of strands of cells which it may be difficult to differentiate microscopically from the normal tissue. In such cases the diagnosis is most readily made from a naked-eye examination.

CARCINOMA

Carcinoma is the commonest variety of malignant disease. It occurs in all races of mankind and in many species of animals. In England and Wales one woman in eight and one man in eleven above the age of 35 years dies of cancer.

A carcinoma is a tumor composed essentially of epithelial cells which tend to invade the lymph spaces of the surrounding connective tissue.

The *cells* are collected into groups separated by a stroma, which, however, does not penetrate between the individual cells of which the group is composed. In this respect a carcinoma differs fundamentally from a sarcoma, as epithelium differs from connective tissue.

The *stroma* varies greatly in amount and consistence, and plays an important part in determining the physical characters of the growth. It is called into existence by the stimulus of the epithelial cells, and, although secondary in character, it is nevertheless essential for the welfare of the neoplasm. If the thrombus which forms around an embolus of carcinoma cells impacted in a capillary does not become invaded by a stroma, the cells soon die and fail to form a tumor. A similar occurrence has already been described in connection with the experimental transplantation of tumors. On the other hand the connective tissue reaction may be so intense that the stroma chokes and kills the epithelial cells.

Extension.—A carcinoma generally grows along lymph spaces or vessels, and it may be possible to demonstrate the lymphatic

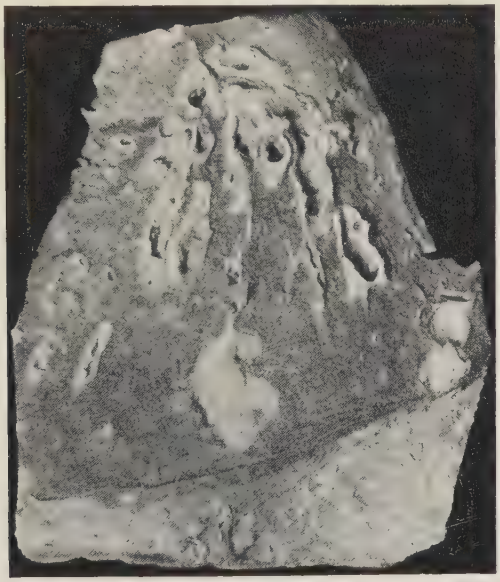


FIG. 42.—Secondary carcinomatous deposits in lung.

endothelium around the cell mass. On looking at a microscopic section of a carcinoma it appears as if there were numbers of separate masses. It must be remembered, however, that the tumor forms one mass with branching extensions which are cut across in the section so as to give a fictitious appearance of multiplicity.

The nearest *lymph glands* are involved by the process of permeation, the cancer cells growing along the lymphatic vessel; or emboli may be carried by the lymph stream and lodge in the gland. It is of great practical importance to remember that the glands are not enlarged in the early stages, although they may be packed with carcinoma cells. On section the gland is seen to contain a small white nodule, which later involves the whole gland.

Metastases are set up in distant parts by the lymph or by the blood stream. The chief means of spread of carcinoma is the lymphatics, as that of sarcoma is the blood vessels, but a carcinoma may at any time invade a vessel and enter the blood stream.

There are remarkable differences in the liability of different forms of cancer to produce metastases. Squamous-celled carcinoma involves the neighboring lymphatic glands, but rarely the distant viscera. Carcinoma of the alimentary canal commonly involves the liver through the portal vein, but seldom more distant organs. The lungs are the common site for metastases from carcinoma of other glands. In some cases of carcinoma of the prostate, thyroid, and breast the metastases show an extraordinary preference for the osseous system, so that most of the bones of the skeleton may show deposits while the other organs may remain free. Tumors of the adrenal (hypernephroma) may display a similar peculiarity.

Metastases reproduce, as a rule, the structure of the primary growth with remarkable fidelity, even to the extent of showing the same type of degeneration, as in the case of a colloid cancer. Occasionally, however, there may be marked differences. A carcinoma of the breast with few cells and abundant stroma may appear in a lymph gland as a highly cellular growth with scanty stroma.

Secondary Changes.—*Fatty degeneration and necrotic softening* are common, especially in the soft cellular forms. *Hemorrhage* may accompany the degeneration, but is not so common as in sarcoma. *Colloid degeneration* may occur, especially in the alimentary canal and the breast, giving rise to the form known as colloid cancer. *Ulceration* is common in superficial cancers, as those of the skin, alimentary canal, uterus, and bladder. The characteristics of such ulcers are illustrated on page 93. Ulceration is always accompanied by *septic infection*, and the condition of the patient usually takes a marked turn for the worse, with the development of cachexia, anemia, and other general symptoms of malignancy. If the infected area can be extirpated and cleansed there may be marked improvement in the clinical condition, even though removal of the whole tumor be impossible. In the serious consequences of secondary infection malignant disease bears a close resemblance to tuberculosis.

Classification.—Epithelium occurs in so many forms, and the divergencies from the normal in carcinoma are often so great, that to give a simple and at the same time satisfactory classification is a next to impossible task. For practical purposes, however, the carcinomata may be divided into two great groups.

1. *Squamous-celled carcinoma*, commonly called epithelioma, arising from squamous stratified epithelium in the skin, esophagus, vagina, etc.

2. *Glandular carcinoma.*

(*a*) *Adenocarcinoma*, so called because of the tendency to form distinct glandular acini. It arises from columnar-celled mucous membranes and the tubular glands in connection with these, and is there-

Metastatic carcinomatous nodules in pleura.

fore also known as columnar-celled carcinoma. It usually occurs in the alimentary canal, but may be found in acinous glands such as the breast.

(*b*) *Carcinoma simplex*, arising from acinous glands such as the breast; also called spheroidal-celled carcinoma owing to the spherical shape of the cells, although these are more often compressed by the stroma into polygonal forms. The cells do not tend to form acini, but grow in solid masses or strands, often arranged in groups or alveoli by the disposition of the stroma. If the stroma is abundant and the cells scanty the growth is called *scirrhous*, if highly cellular with scanty stroma *medullary* or *encephaloid*. A scirrhous carcinoma is not, however, necessarily a carcinoma simplex, for a similar superabundance of stroma may also occur in an adenocarcinoma.

Colloid cancer is a term applied to a carcinoma the cells of which have undergone colloid degeneration. It is not a separate form, and although commonest in the adenocarcinomata of the alimentary canal it may occur in a carcinoma simplex of the breast.

FIG. 43.—Epithelioma following ulcer. (Keen's Surgery, Vol. I).

EPITHELIOMA

An epithelioma should of course be called a squamous-celled carcinoma, for all epithelial tumors are epitheliomata, but the term is of such common usage that it cannot be dispensed with. Epitheliomas occur wherever squamous or transitional epithelium is found, and as such epithelium differs depending on whether it occurs in the skin, the esophagus, or the bladder, so the epithelial growths in these regions present differences of structure. They all have certain features in common, however, by which they can be recognized.

The favorite site for an epithelioma is a place where two different types of epithelium come together, such as the lip, the nostril, the eyelid, the upper end of the esophagus, the penis, or the vulva. In other positions it is usually associated with some form of chronic irritation, often developing at the edge of a chronic ulcer.

A typical epithelioma, such as occurs on the lower lip, begins as a slight thickening or a small nodule. Ulceration usually occurs, the ulcer refuses to heal, and is covered with a crust. The nearest lymphatic glands become enlarged.

Microscopically solid columns of epithelial cells are seen growing down into the dermis, separated from one another by connective tissue. These expand into bulbous masses which on section may appear quite detached. In course of time the cells nearest the center of these masses, being the oldest, undergo the same degenerative changes as are usual in normal surface epithelium, granules of eleidin appear in their cytoplasm, and finally the central cells become converted into a hyaline structureless mass of keratin, a process of keratinization or cornification. A mass is then formed in the center of which is a horny

Fig. 44.—Epithelioma of hand. Removed from an insane patient.

material, further out are granule-laden cells, and the periphery is formed by normal-looking squamous cells, often presenting the characteristic "prickle-cell" appearance, and arranged in a somewhat concentric manner. These peculiar masses are known as "cell-nests" or "epithelial pearls," but although highly characteristic of an epithelioma they are often absent in rapidly growing tumors, and in the esophagus and bladder where cornification does not normally occur. The stroma is commonly infiltrated with inflammatory cells, lympho-

cytes, and plasma cells derived from the tissue, whose presence is due to the irritation produced by the epithelial masses. They probably represent a defense reaction on the part of the body.

Such are the features of a typical epithelioma of the skin. In the tongue and esophagus extensive ulceration is a marked feature, and cornification and cell nests are usually absent, but they may occasionally be found.

Carcinoma of the cervix uteri, one of the commonest and most dangerous of all forms of carcinoma, is of the epitheliomatous type,

Fig. 45.—Epithelioma of foot. The patient had been treated for a long time with Christian Science.

but differs from the typical epithelioma elsewhere. It is composed of thick irregular strands and masses of stratified cells showing numerous mitotic figures, but there are no cell nests nor cornification. The stroma is plentifully infiltrated with plasma cells.

In organs lined by transitional epithelium such as the bladder the epithelioma consists of irregular masses of transitional cells, but there are no prickle cells nor cell nests. Cornification is absent.

Broders distinguishes four different grades of epithelioma of the skin. The distinction is based upon the degree of differentiation of the cells, which itself is inversely proportionate to the degree of malignancy. Most epitheliomas show both differentiated and undifferentiated portions; it is the proportion of the one to the other which is of importance

Fig. 46.- Epithelioma of skin.

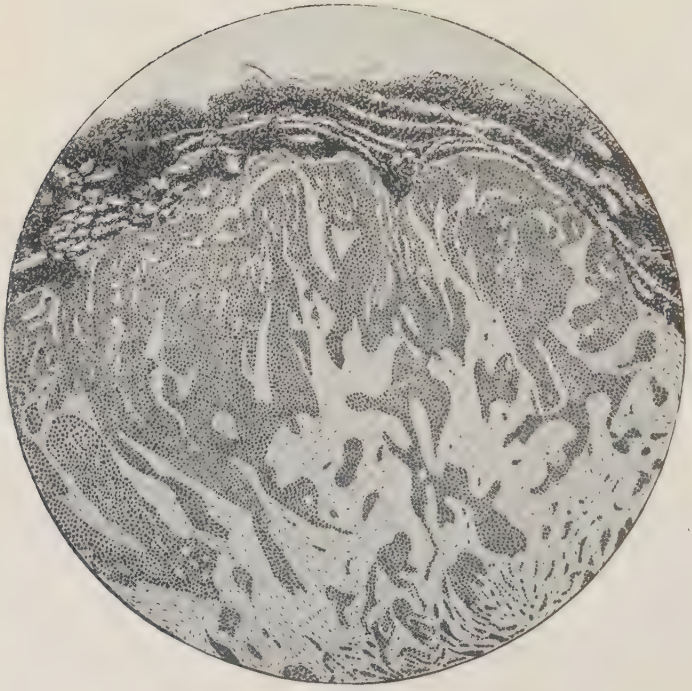


Fig. 47.—Epithelioma; inflammatory reaction on surface.

Broders found as the result of his studies that he was able to give a much more accurate prognosis. A large proportion of undifferentiated cells with round nuclei containing a single deeply staining nucleolus, what Broders calls "one-eyed cells," places the tumor in grade 4, with a hopeless prognosis. Out of 256 cases of epithelioma of the skin the known deaths from epithelioma were: grade 1—0; grade 2—61 per cent; grade 3—85 per cent; grade 4–100 per cent.

An epithelioma may occasionally originate in an organ lined by columnar epithelium. This is an example of metaplasia; for instance in the gall-bladder, where the occurrence is commonest, the columnar epithelium reverts to the squamous type, often as the result of irritation from calculi, and an epithelioma develops upon this debased epithelium.

Rodent Ulcer.—There is one form of squamous-celled carcinoma of the skin which differs in important particulars, both clinical and histo-

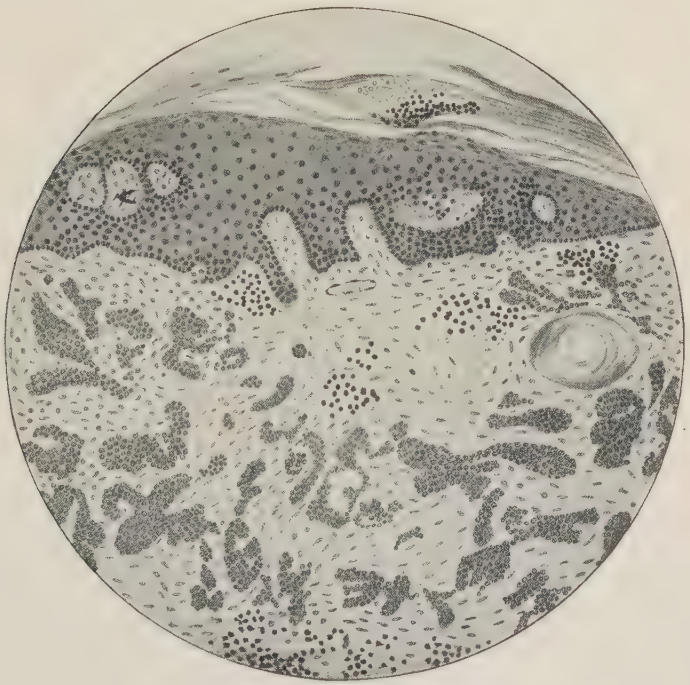


FIG. 48.—Rodent ulcer. Club-shaped, deeply situated masses of darkly staining cells.

logical, from the ordinary epithelioma. It occurs on the upper part of the face, about the cheek, nose, eyelid, or ear, but *not* at the junction of skin and mucous membrane, and although it may eventually produce the most terrible destruction and disfigurement through its eroding action, it grows very slowly, often over a course of many years, the glands are not involved, and metastases are not set up. It

is called rodent ulcer, or by some basal-celled carcinoma under the belief that it originates from the basal layer of the epidermis. Others hold that it arises from the sebaceous glands or the hair-follicles. The former view is probably correct. It consists of solid masses or columns of cells growing downwards into the dermis. The columns all reach to about the same level, have a characteristically club-shaped appearance, and the connection with the epidermis can rarely be seen in a given section. The cells are small and compact, with scanty protoplasm and a darkly staining nucleus, and are very different in appearance from the pale inflated cells of an epithelioma. There are no prickle cells, cell nests, nor cornification. The layer of cells on the outside of the mass are frequently columnar in shape.

Adamantinoma.—This peculiar and rare tumor may be considered in this place, for it probably arises from the enamel organ, an epithe-

Fig. 49.—Adamantinoma, showing the gland-like appearance produced by degeneration of the center of the masses.

lial structure, although it is considered by some to originate in the paradental epithelial débris. The tumor may be solid or cystic. It distends the alveolar border, being surrounded by a thin capsule of bone. Although an innocent growth, it may eventually rupture the capsule, and extend into the antrum or the orbit. As a rule it remains small, but may occasionally attain a considerable size. Indeed Ewing

mentions a case where the mass in the upper jaw was as large as a child's head.

The microscopic structure varies considerably, but it usually consists of strands and masses of epithelial cells, the center of the masses becoming hollowed out so as to give a glandular or cystic appearance. The deepest layer of cells is almost cylindrical. The general appearance is well shown in Fig. 49.

ADENOCARCINOMA

A columnar-celled carcinoma may arise either from mucous membranes or from glands lined by columnar epithelium. It occurs

FIG. 50.—Adenocarcinoma of stomach. There is a very sudden change from the normal mucosa to the wildly proliferating epithelium. The cells of many of the new glands stain darkly.

especially in the stomach, large intestine (cecum and rectum), gall bladder, pancreas, uterus, and prostate.

The tumor may conveniently be studied in such an organ as the stomach. Two main forms occur, the nodular which projects as an ulcerated mass, often polypoid in form, into the stomach, and the sessile which infiltrates the walls and produces a localized thickening. The former presents the more characteristic appearance. The nature of the mucosa changes at the edge of the growth with dramatic

suddenness. The glands become highly irregular, with numerous branching processes, and may be filled with epithelial cells. The cells stain more darkly than those of the normal mucosa, frequently show mitosis, and are no longer limited by a smooth basement membrane, but wander out into the surrounding stroma. Most characteristic of all, glands are found where they should never normally occur, namely deep to the muscularis mucosa. The stroma is densely infiltrated with inflammatory cells.

In the sessile variety the glandular arrangement may be lost, the stroma may be so dense as to be scirrhous in type, and the cells may be arranged as solid strands, so that the growth has become a carcinoma simplex. Such growths of the stomach illustrate very well the essential similarity between the two types of glandular cancer, the adenocarcinoma and the carcinoma simplex.

FIG. 51.—Adenocarcinoma, metastasis in liver from primary growth in stomach.

Metastases are very common in the neighboring mesenteric glands, in distant glands, especially the supra-clavicular group, and in the liver.

Colloid degeneration is of not infrequent occurrence in the stomach and large intestine. Large masses of gelatinous new growth are formed rather like sago pudding, with great thickening of the stomach wall. Such a condition is called *colloid cancer*, but the term is

undesirable if it gives rise to the belief that this is a special variety of carcinoma. Curiously enough the metastases have the same colloid appearance as the parent growth.

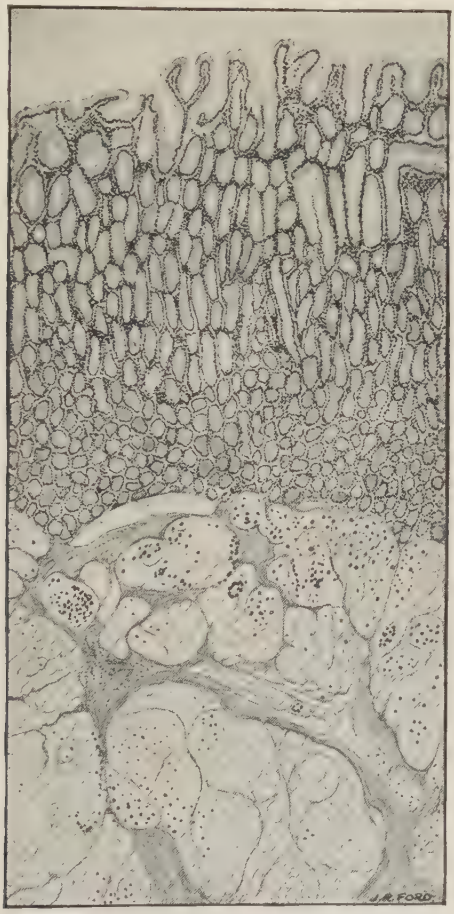


FIG. 52.—Colloid cancer of stomach. The submucosa is invaded by carcinoma cells which have undergone an extreme degree of colloid degeneration.

CARCINOMA SIMPLEX

A carcinoma simplex, like an adenocarcinoma, is derived from glandular epithelium. Speaking generally, while an adenocarcinoma grows from the columnar epithelium of mucous membranes, the carcinoma simplex arises from the cubical epithelium of solid glands. We have seen, however, that the same epithelium may at one time give rise to an adenocarcinoma, at another to a carcinoma simplex.

As the most important site clinically of a squamous-celled carcinoma is the cervix of the uterus, and of an adenocarcinoma the stomach, so by far the most important position of a carcinoma sim-

plex is the breast. It may also be found in the prostate, ovary, thyroid, liver, and alimentary canal.

The cells are more or less spheroidal, but are often distorted by the pressure of the stroma so as to become polygonal. The cytoplasm is abundant, and the nucleus stains darkly. The stroma varies greatly in amount and density, imparting similar variations to the gross character of the tumor.

In the *scirrhous* form the dense, scar-like stroma is so abundant as to constitute the greater part of the tumor, and the cells are scanty, and arranged in small groups or columns, or they may be actually in single file growing along the lymph spaces. Mitotic figures are

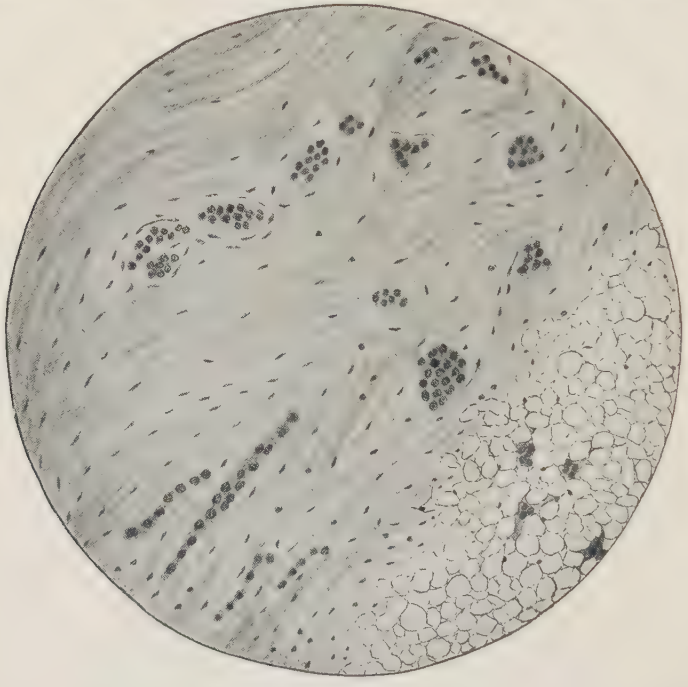


FIG. 53.—Scirrhous cancer of breast. The type of growth is carcinoma simplex, the cells being arranged in solid masses and columns. The malignant cells are invading the fat.

not common. The mass is densely hard, and when cut imparts to the hand a gritty sensation, recalling that of an unripe pear.

In the *medullary* or *encephaloid* variety the cells are rapidly growing, show numerous mitotic figures, and are collected into large masses separated by a scanty and delicate stroma. Areas of degeneration and necrosis are common, although rare in scirrhous growths. But one part of the tumor may show one type, another the other. Or a scirrhous cancer may begin to grow rapidly and become medullary in type. Or the metastases of a scirrhous growth in a gland may assume the medullary form, although usually repeating the scirrhous structure.

NERVOUS TISSUE TUMORS

The nervous system is developed from epithelial cells which line the neural canal, and from these cells both the nerve cells and the neuroglia are formed. Thus the neuroglia, although resembling connective tissue in structure and function, is epithelial in origin. During development large numbers of cells migrate to form the sympathetic nervous system, and many of these penetrate the medulla of the adrenal, so that tumors composed of nerve cells may arise in that organ. As might be expected, two varieties of tumor may be met with in the nervous system and its derivatives, the glioma, a common tumor arising from the neuroglia, and the neurocytoma or neuroblastoma, a rare tumor arising from the nerve cells or neurocytes.

Glioma.—The glioma occurs in the central nervous system and in the retina. It is an innocent tumor in the sense that it is slow growing

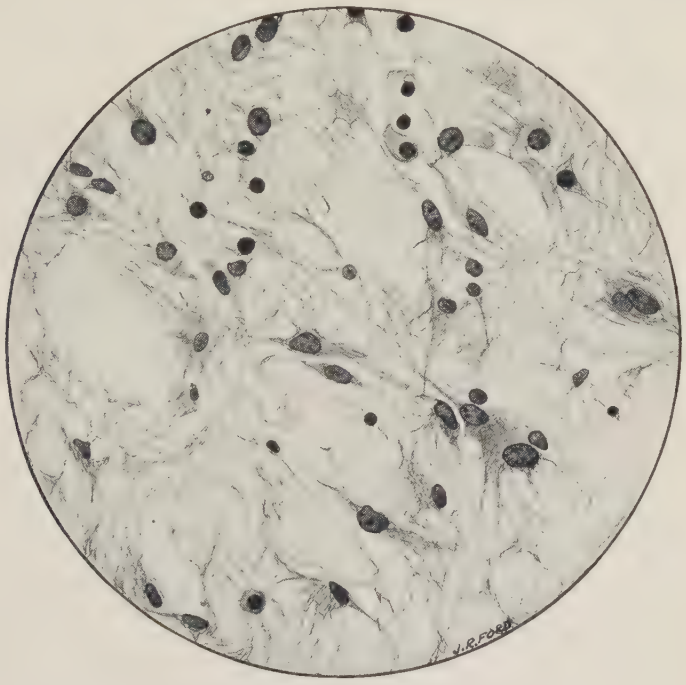
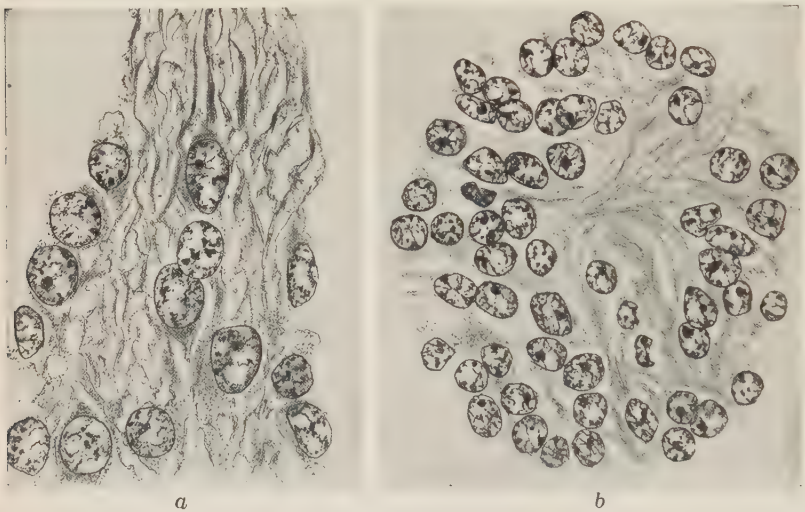


FIG. 54.—Glioma. Glial cells and fibers.

and does not set up metastases, but it is invasive, and will result in the death of the patient. Occasionally it may take on malignant characters, grow rapidly, and show an almost wholly cellular structure. It is difficult or impossible to distinguish such growths from true sarcomata. It is whitish-grey in color, soft in consistency, and fades so gradually into the surrounding brain substance that no line of demarcation can be made out, a characteristic which makes

operative treatment very difficult. Degeneration and softening is liable to occur, so that cysts are frequently present.

Microscopically the growth consists of rounded cells, usually small in size, with a deeply staining nucleus. Between these there is a fine network of neuroglia fibers, which can be stained differentially, and thus form the means by which the nature of the growth can be recognized. The differential stain can only be used on quite fresh tissue, so that it is of much greater use in surgical material than in that removed post-mortem. Occasionally the cells may have a rosette-like arrangement, or may be grouped round a central lumen giving a glandular appearance. This is best seen in tumors of the eye.



a *b*

FIG. 55.—Neuroblastoma of the adrenal gland showing bundles of nerve fibrils. (Mallory.)

Neuroblastoma.—Tumors arising from nerve cells are commonest in the medulla of the adrenal, but may be met with in the brain. They generally occur in young children. They are composed of nerve cells and fibers. The cells, which are quite unlike the typical nerve cells of the cerebrum, are small and round, and are often arranged in rosette form. It is the fibers, however, which are characteristic of the tumor, for they can be stained with a differential nerve fiber stain, and thus distinguished from neuroglia or connective tissue fibers. These tumors are usually malignant, and give rise to metastases.

The condition commonly called an *amputation neuroma* is not a tumor at all. It is a bulbous swelling at the end of a cut nerve due to hyperplasia of nerve fibers and connective tissue.

BONE MARROW TUMORS

Myeloma.—A myeloma is a rare tumor arising simultaneously from the bone marrow of the vertebræ, the ribs, and the cranium.

Why such growths should arise simultaneously, or whether one is primary and the other secondary, has never been determined. The masses are soft in consistency, reddish grey in color, and weaken the bone so that spontaneous fracture may occur.

Microscopically they consist of rounded cells separated by a delicate stroma. The nature of the cells is uncertain, but in some cases they are supposed to arise from myelocytes, in others from lymphoid cells. In the latter the cells of the tumor closely resemble plasma cells. In one case of multiple myelomata involving the skull the cells were large enough to resemble myelocytes. On applying the oxydase reaction, however, the writer found that not one of the cells showed the characteristic granules, whereas the polymorphonuclear leucocytes within the blood vessels of the tumor showed them very beautifully. This reaction is of the greatest value in distinguishing between the myelocyte and the lymphocyte series of cells.

The urine in about half the cases contains a peculiar albumose called Bence-Jones protein. This appears as a cloud when the urine is heated to 55° C. but disappears when 85° is reached, reappearing again when the urine is cooled.

It is probable that a close relationship exists between myeloma and the various forms of leukemia, in which the marrow cells may form tumor-like masses in the viscera in addition to those circulating in the blood. In myeloma, however, the leucocytes do not display any constant change.

Chloroma is a very rare tumor-like condition occurring in young people, which forms a link between myeloma and leukemia. Masses of a bright green color are present in the periosteum of the bones especially of the face and head. The color fades rapidly after death, and the pigment has not been isolated. The blood usually shows a condition of leukemia, the type not being constant.

ENDOTHELIAL TISSUE TUMORS

In the whole subject of oncology there is no group of tumors regarding which greater doubt exists than those arising from endothelium. The group of the endotheliomas is a rubbish heap on which are thrown all those tumors of uncertain nature and origin which do not fall into the well recognized classes of neoplasms. One of the great stumbling blocks is the fact that there is no general agreement as to which tissues are in truth endothelial. It is generally admitted, however, that the lining of blood vessels, lymphatics, and the dura mater is endothelial in nature, and that the pleura and peritoneum may possibly be included also.

The endothelial cell is a large flat cell with a large oval nucleus, but in a tumor it may be elongated, cubical or polygonal. It may occur in the following forms: (1) as a lining of vessels, (2) as concentric masses often showing a whorled arrangement, and (3) as solid columns of cells. An endothelial growth is usually innocent, but it may assume the infiltrative character of malignancy.

For our present purpose endothelial tumors may be divided into:

1. Endotheliomas.
2. Endothelio-hemangiomas, commonly called angiomas.
3. Endothelio-lymphangiomas, commonly called lymphangiomas.

Endothelioma.—An endothelioma occurs most frequently in the dura mater. It may occasionally arise from the pleura or peritoneum, and some tumors of doubtful nature, especially those in the parotid region, are often included in the same group.

The dura mater tumor grows from the inner surface of the dura lining the skull, may attain the size of a tangerine orange, and presses upon the brain producing the symptoms of a cerebral tumor. It is firm in consistence, and is composed of elongated cells which have a characteristically whorled arrangement. They may be arranged round blood vessels, or no such arrangement may be evident. Especially in the case of small tumors there may be a hyaline degeneration of the whorls, with the deposition of lime salts, giving rise to a *psammoma*. Such a tumor shows numerous structureless bodies of concentrically laminated appearance, the psammoma bodies, recalling the corpora amylacea seen in the prostate and other glands.

The growths in the pleura are flat, diffuse tumors, slightly raised above the surface, and consist of an irregular network of epithelial-like cells, sometimes showing an alveolar arrangement. These tumors are usually innocent, but they may occasionally infiltrate.

It has been the custom to regard the peculiar tumors occurring in the parotid region as endotheliomas. These tumors often consist of sheets or cords of cells resembling those of an endothelioma. Other types of cell, however, are always present, and these may dominate the picture. Cartilage cells are particularly abundant, and the tumor may appear to have the structure of a pure chondroma. The condition is to be regarded as a developmental tumor, a form of teratoma, rather than an endothelioma (see page 227). The tumor forms a circumscribed lobulated mass, superficial to the parotid gland, and often situated just below the ear. It grows slowly, and may attain an enormous size without displaying malignant characteristics, but at any time it may commence to infiltrate. Similar growths may occur in the submaxillary region, lip, and palate.

Angioma.—An angioma (hemangioma) is a tumor consisting of new-formed blood vessels. Frequently, however, it is difficult to say if a collection of vessels is a true neoplasm or merely a dilatation of previously existing vessels (telangiectasis). Two forms of hemangioma are recognized, the capillary and the cavernous.

Capillary Angioma.—This consists of a network of capillaries filled with blood. The lining cells, which are large and swollen, may be several layers in depth, and the lumen may be very small, sometimes containing no blood. The cells may proliferate to such an extent that they obliterate the lumen, and the tumor then resembles an endothelioma. The cells may be arranged in whorls, especially

around the blood vessels. It has recently been shown that the first stage in the formation of vascular spaces from the mass of proliferating cells is the development within each cell of a vacuole, which gradually enlarges until the entire cell becomes flattened. In many of the cells

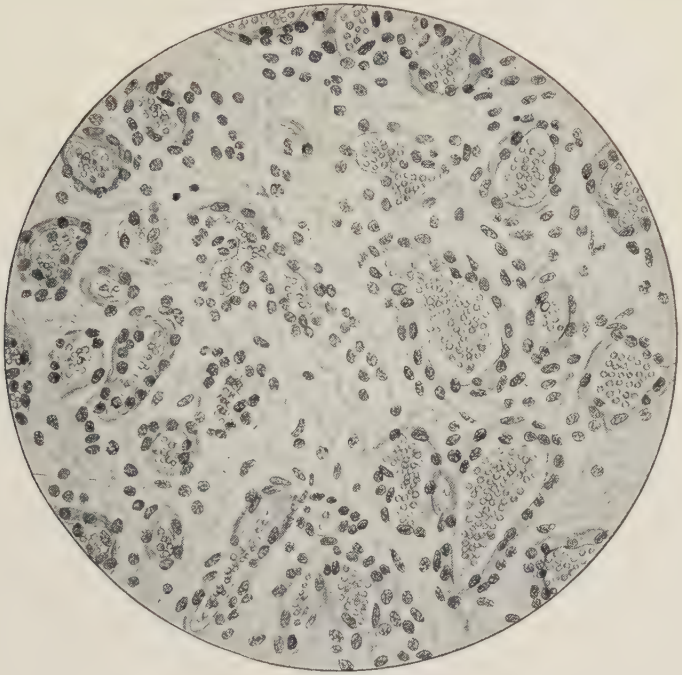


FIG. 56.—Capillary angioma.

FIG. 57.—Cutaneous angioma.

the wall gives way so that the vacuoles coalesce, and new blood spaces are thus formed, at first irregular in shape, but later conforming to the regular form of capillaries.

The common site is the skin, but it may occur in the mucous membrane of the nose, lip, tongue, gum, or rectum, in which latter position it may occasion severe hemorrhage.

A cutaneous angioma is usually a bright red, sharply defined patch, not raised above the general level, but it may present a somewhat

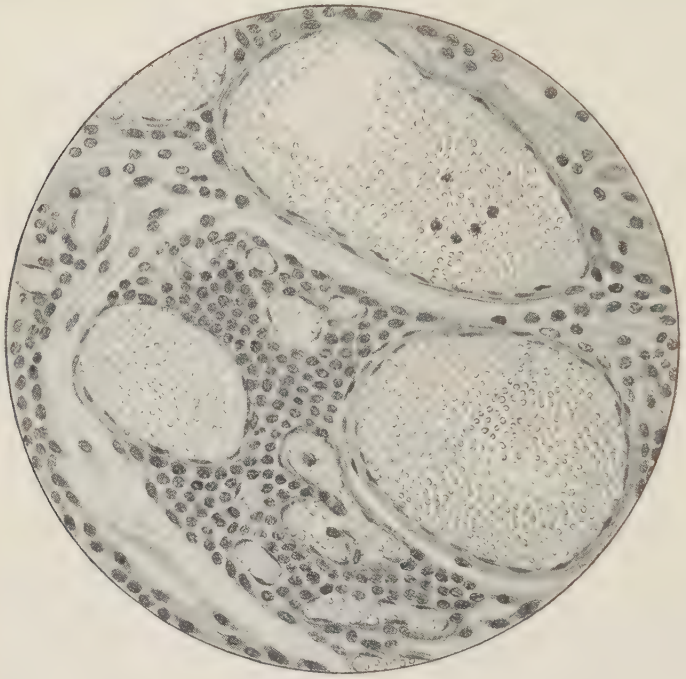


Fig. 58.—Cavernous angioma.

velvety surface. It is generally present at birth, and from a minute red spot it may spread to cover a large surface. The favorite position is the face or head, where it often follows the distribution of the fifth

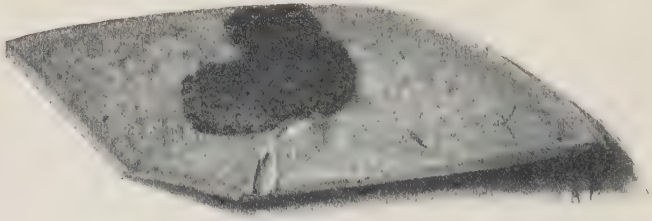


Fig. 59.—Cavernous angioma of the liver. (MacCallum.)

nerve, and it is almost always strictly unilateral, stopping short at the middle line.

These angiomas are commonly known as port-wine stains, birth marks, or strawberry marks. In England the term nevus is used, but

this should be confined to an entirely different form of neoplasm also occurring in the skin (see below).

Cavernous Angioma.—The structure of this tumor is that of erectile tissue. It resembles a fine sponge, and on section is of a deep red color. It consists of large blood spaces or sinuses lined with endothelium. The common site is the liver, where it may be multiple. It is also found in the skin in various regions, including the lip, where it forms a raised mass, often of distinctly higher temperature than the surrounding structures, the overlying skin generally shows a bluish tinge, and gentle pressure may succeed in emptying the tumor. It may infiltrate the subcutaneous tissue and underlying muscles, and I have seen the most alarming hemorrhage result from an ill-advised attempt at removal in such a case.

PIGMENTED TUMORS

Tumors containing varying amounts of pigment form one of the most interesting groups of neoplasms. Two main varieties may be recognized, the mole or nevus, an innocent formation, and the melanoma or melanotic sarcoma, a markedly malignant growth.

The *origin* of the tumor cells for long has been a matter of hot dispute, nor indeed has the question yet been decided. Unna was the first to point out the close relationship which the cells bear either to the basilar layers of the epidermis or to such derivatives of the epidermis as the hair follicles or the sweat glands. In the congenital moles of young children one can trace different stages in the development and segregation of the cells of the epidermis into those of the tumor. Many malignant melanomas present such intimate relationships with the epidermis and such insensible gradation from the one into the other that it is impossible to persuade oneself that the tumor is not of epithelial origin.

On the other hand there is much to be said for the development of at least some of these tumors from the special mesoblastic pigment cells known as melanoblasts or chromatophores. If this be true the tumor will be more deserving of its common name of melanotic sarcoma. The apparent epidermal origin in many cases is accounted for by the invasion of the epidermis from below by the mesoblastic cells.

No one theory can be made to provide a satisfactory explanation for all cases. It may be that some of the tumors have one mode of origin, whilst others have another.

Nevus.—The nevus or mole may be pigmented or non-pigmented; the former is common, the latter rare. The pigmented mole may be almost level with the surface, or may be markedly raised. It may be grey, brown, or black in color. The surface is often covered with coarse hairs. Whilst it may be found in any part of the body it usually occurs on the face, the neck, or the back. Those moles situated on exposed parts are most liable to malignant change, but even on covered parts of the body, as the back or the foot, they may be subject

to irritation, and such moles are always a source of danger. The condition must be regarded as a congenital one, but the mole may not be apparent at birth, only becoming evident later in childhood.

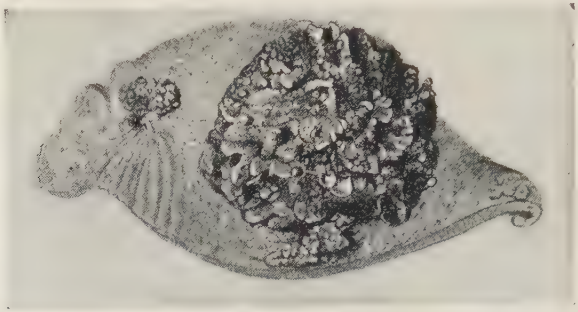


FIG. 60.—Pigmented nevus.

The great majority of moles fortunately pursue an absolutely innocent course, growing slowly for a long period, then becoming quiescent, and finally undergoing retrogressive and fibrotic changes.

FIG. 61.—Pigmented nevus, showing masses of nevus cells in papillæ of corium.

As the result of irritation, however, or of injudicious and incomplete surgical interference, they may at any time develop malignant characteristics.

Microscopically we may distinguish the congenital mole of infants and children and the mole occurring in adults. In the *infantile* form the cells of the deeper layers of the epidermis or those of the hair follicles and sweat glands become swollen, their cytoplasm clear, and their nuclei hyperchromatic. These cells become isolated and form clumps in the underlying tissue. Numerous pigment granules frequently are found in these cells. As the cells become isolated from the epidermis they gradually lose their pigment and enter upon a period of quiescence. The sequence, therefore, is proliferation with pigmentation, depigmentation, and quiescence. In the *adult* form the epidermis is seen to send elongated processes down into the corium, and in the intervening papillæ there are alveolar groups of clear cells with dark nuclei. Some of these nevus cells may be colorless, whilst others are deeply pigmented. As a rule no connection with the epidermis can be seen, and the picture is one of quiescence, but occasionally the

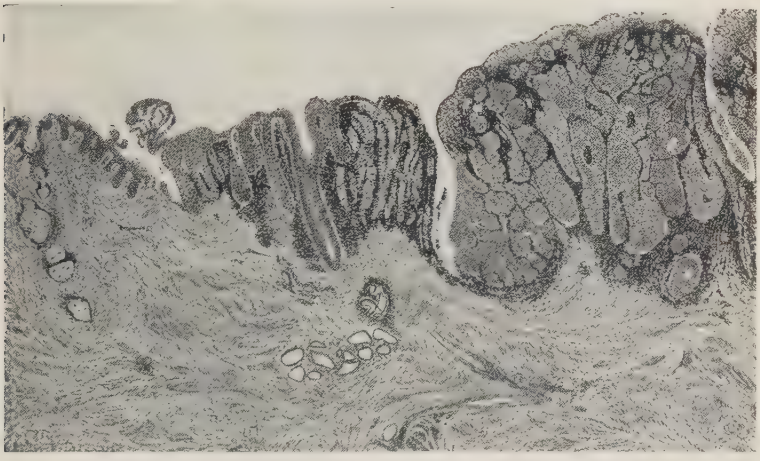


Fig. 62.—Nevus of skin.

process of derivation from the epidermis may apparently still be going on.

Melanoma.—A melanoma or melanotic sarcoma is a malignant pigmented tumor, which in the great majority of cases arises from a pre-existing pigmented mole, but may originate in the choroid or iris, and rarely in other positions such as the brain, meninges, adrenal, and ovary. The nodules are of a dark brown or black color.

The *metastases* are the most important feature of a melanoma. The primary growth seldom attains a great size, nor does it occasion any serious clinical disturbance. It is the widespread metastases which constitute the lethal factor. These frequently first appear in the skin, where they form numerous small firm nodules which may or may not be pigmented. The spread may be either by the blood or the lymph stream. As the result of blood infection there may be numerous

secondary growths in the lungs, liver, kidney, brain, and many other organs.

Even after the tumor has become definitely malignant, as shown by enlargement and an increase of pigmentation, the subsequent history may vary greatly. In many cases the spread is chiefly by the lymph stream, with involvement of the regional lymph nodes. Sampson Handley, in his Hunterian lecture on melanomata, has emphasized the importance of removal not only of the neighboring glands but of the intervening lymphatics which are also implicated. Thorough treatment of such a nature at this stage of the disease may result in a complete cure. Occasionally the disease, although malignant, may

FIG. 63.—Melanotic growths of skin in various stages of development. The primary growth was in the heel.

remain localized for a number of years, only to become generalized in the end.

Although melanomata are usually regarded as tumors of great malignancy, remarkable examples of at least temporary immunity sometimes occur. Pearce Gould records a case in which the skin over the greater part of the body was covered with melanotic nodules, all of which with the exception of two disappeared in the course of a few weeks. Six months later cutaneous nodules again appeared, and the patient died after being confined to bed for only three or four days.

Two cases which I published some time ago also serve to show how little the general health may be interfered with even when the tumors are widespread in their distribution. One of these was an old man who for seven years had suffered from melanoma which had originated in the heel; for three years there had been distant glandular involvement, with blood spread for one year, and yet the patient appeared to be in excellent health. In the other case the disease first appeared in the right axilla, although there was a history of some growth being

FIG. 64.—Secondary deposit of melanotic sarcoma in the lung.

removed from the interscapular region seven years before. The patient remained well for six months, when numerous dark nodules appeared on the skin of the chest and the abdominal wall. Next year he developed an intussusception due to the irritation of a melanotic mesenteric gland. Some months later he complained of a sore throat, and it was found that the tonsils were converted into two large black masses. The microscopic structure of all the growths was that of a typical melanoma. All this time the patient remained in robust

health, and continued his work as a farmer. He died somewhat suddenly in the following year.

Melanemia and melanuria are both occasional occurrences. The serous membranes and the lining of the blood vessels may become pigmented.

Microscopically the picture is a varied one. The signs of the malignant transformation are usually readily recognized. The tumor cells are no longer confined to the usual site but are evidently spreading to the deeper tissues. There is an increased vascularity, the cells have become larger, the nuclei are hyperchromatic, and mitotic figures

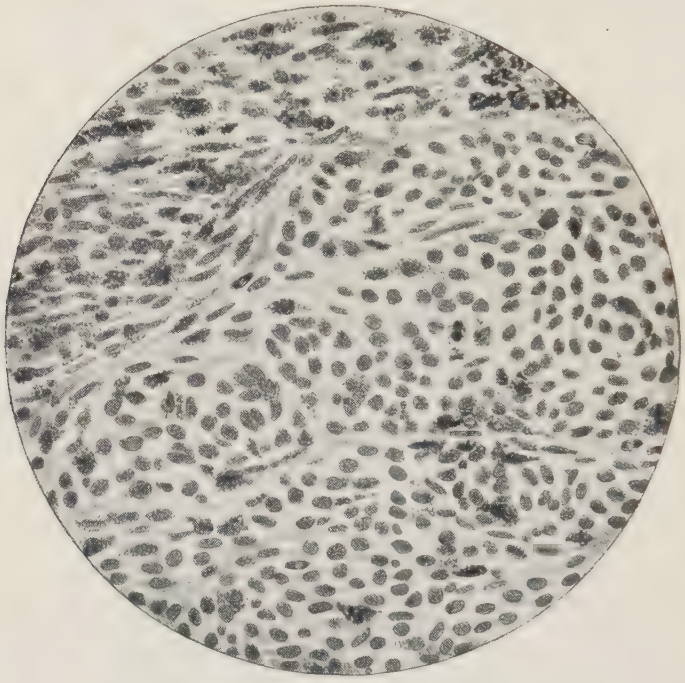


Fig. 65.—Melanotic sarcoma showing pigment granules and mitotic figures.

can be seen. Pigmentation is usually marked, but this cannot be regarded as an invariable criterion. In one part of a section the cells may be loaded with yellow pigment, whilst in another part all of the cells may be pigment free. The cells for the most part are large and epithelial-like, polyhedral in form, closely applied to one another, and may appear as if wrapped around each other. An alveolar grouping is usually well marked, the groups being separated by a fine stroma. In one of our cases the cells in one part of the tumor had what appeared to be a tubular arrangement whilst in another part there was a close resemblance to a hypernephroma. Instead of assuming a polyhedral form many of the cells may be elongated and spindle-shaped, resembling those of a single-celled sarcoma.

In the metastases the cells may be of the round or the spindle form. The degree of pigmentation varies greatly. In a case of diffuse melanomatosis of the meninges we found that the cells in the subarachnoid space were loaded with pigment, whilst those in the perivascular prolongations of that space in the cortex were absolutely devoid of it. The criterion for diagnosis should therefore be the type and arrangement of the cells rather than the presence of pigmentation.

HYPERNEPHROMA

A hypernephroma is a tumor consisting of adrenal tissue, occurring usually in the kidney, but occasionally arising from the adrenal cortex, although the latter is better termed an adrenal carcinoma, and in rare cases growing in the liver, spermatic cord, and other positions. It is supposed to originate from the adrenal "rests" which Grawitz in 1883 showed may occur in the kidney, liver, pancreas, broad ligament, and spermatic cord.

These tumors may display little sign of malignancy for a considerable length of time, but at any time they may take on a malignant character, growing along the renal vein and even up the vena cava, and setting up widespread metastases which sometimes display a marked predisposition to attack the osseous system.

Tumors growing from the adrenal in children are often associated with a marked degree of precocious sexual development. This is not seen in renal hypernephromas.

As the gross and microscopic appearances, together with the vexed question as to the origin of these tumors, are fully discussed in Chapter XXIII, they need not receive further consideration here.

CHORIONEPITHELIOMA

The chorionepithelioma is a tumor in a class entirely by itself, for it originates from the cells of another individual, the cells of the chorionic villi of the fetus.

The chorionic villi are normally covered by two layers of cells derived from the ectoderm.

(1) *Langhans' cells*, which are cubical or polygonal cells, several layers in depth, with a very clear cytoplasm and relatively large nuclei. (2) *Syncytial cells*, large multinucleated masses of undifferentiated protoplasm, both the nuclei and cytoplasm of which stain very darkly. These masses lie superficial to the Langhans' layer.

The function of these cells is to invade the maternal blood sinuses, but towards the end of pregnancy they are destroyed. In some cases there may be a *hydatidiform degeneration of the villi*, which become converted into a series of small cysts like hydatids, giving rise to a *hydatid mole*.

Chorionepithelioma of the uterus is always connected with pregnancy, but it is usually preceded by abortion, and in a considerable proportion of cases by the development of a hydatid mole. Only

rarely does it occur in connection with a normal pregnancy, and then after more commonly than during the period. The invasive character of the chorionic epithelium for some reason continues unchecked, and a malignant tumor is the result.

A soft, ragged, fleshy mass develops in the uterus, usually in the fundus. It is extremely hemorrhagic, and consists mainly of blood clot. It can be seen invading the uterine wall.

The further gross and microscopic characteristics, together with the peculiar clinical behavior of the tumor, are considered in Chapter XXVI.

TERATOMATA

A teratoma is a tumor consisting of different tissues or organs derived from more than one primitive germ layer. It may be regarded as an attempted formation of a new individual within the tissues of the patient. The tumors vary from simple cystic structures to complex monsters.

Many theories have been advanced to explain the occurrence of these strange formations. For a full discussion of these, together with a description of the various monsters which may occur, the writings of Adami should be consulted. A probable view is that they are due to displacement of one of the blastomeres formed by segmentation of the ovum. If this occurs early, highly differentiated structures may be formed; if late, only comparatively simple ones. Notwithstanding the complexity and elaborateness of some of the theories which have been suggested to explain the origin of teratomata, it is best to acknowledge that our ignorance on the subject is more profound than our knowledge.

Teratomas may be divided into two classes. (1) Those occurring in the genital glands, the ovary and testicle, in which definite fetal structures may be recognized. It is to these that the term teratoma is usually applied. In rare cases they may occur in other situations, notably at the lower part of the vertebral column, where they form what are known as *sacro-coccygeal tumors*, and at the base of the skull. (2) Those occurring in the salivary glands, especially the parotid, and in the kidney. These so-called "mixed tumors" consist of varied structures, such as cartilage, fibrous tissue, and epithelial elements, which, however, form no recognizable fetal organs.

Teratomas of the Ovary.—These may be cystic, which are common and innocent, or solid, which are rare and malignant.

The dermoid cyst of the ovary is a cystic mass with a tough fibrous wall enclosing a greasy, buttery substance in which are embedded epidermal structures, such as skin, hair, nails, and teeth; brain matter is not infrequently present. In one case which came under my notice there was perfectly formed thyroid tissue containing colloid, and in another there was a small but beautifully developed adrenal gland. The skin, hair, etc., spring from a thickened patch of the cyst wall called the dermoid process. The skin contains numerous sebaceous

glands, from which is produced the buttery material which fills the cavity.

Teratoma of the Testicle.—This tumor is nearly always solid, although on section it usually presents an appearance of very numerous small cysts, giving it a spongy look, so that it used to be known by the name of *fibro-cystic disease* of the testicle. It consists of large numbers of tubules lined by columnar epithelium lying in a fibrous stroma. Bundles of well-developed plain muscle are scattered between the tubules, and masses of squamous epithelium, hair and cartilage may be present, the latter sometimes in such abundance as to simulate a chondroma.

These tumors are usually highly malignant, and metastases occur at an early period.

In rare instances a chorionepithelioma has been known to develop in a teratoma of the testicle.

Mixed Tumors.—These are most commonly found in the kidney, but also in the salivary glands.

The mixed tumor of the kidney develops before the end of the second year, and appears to originate in the pelvis, often producing enormous enlargement of the kidney. Degenerative changes such as hemorrhage and mucoid softening are common. The tumor consists of a groundwork of rounded cells, recalling those of a sarcoma, together with numerous tubules lined by cubical or columnar cells. Cartilage, smooth muscle, and not infrequently striated muscle may be present. It will be seen that these tumors may resemble either a sarcoma or a carcinoma, and it is to such growths that the objectionable terms carcinoma sarcomatodes and sarcoma carcinomatodes have been applied.

Inclusion Dermoids.—Reference may be made in this place to inclusion dermoids in order to distinguish them from the dermoid tumors occurring in the genital glands. These tumors may be divided into implantation dermoids and congenital dermoids.

Implantation Dermoids.—If a small portion of skin is implanted in the deeper tissues as the result of trauma, there may be formed a cyst lined by epidermis. If only the epidermis has been implanted the lining will be smooth; if the dermis is also included the cyst wall will contain papillæ. These cysts usually occur in working people on exposed parts of the body, such as the palm of the hand or the sole of the foot.

Congenital Dermoids.—These occur in situations where inclusion of dermal tissue is apt to occur in the course of development, namely along the line of the embryonic fissures. They are met with in the scalp, neck, back, and along the middle line of the chest and abdomen. Many of these tumors arise from the *branchial clefts*, particularly the second, a portion of skin being included during the process of closure. *Mediastinal dermoids* are rare tumors found in the anterior mediastinum or within the lung. In some cases the patient has coughed up hair as well as sebaceous material. These growths are

probably derived from the third branchial cleft. Other positions in which congenital dermoids occur are the *skull* (growing from the dura mater along the line of the tentorium cerebelli), the orbit, and the pharynx (including the thyroglossal duct and the track leading from the pharynx to the pituitary body).

The tumors are usually cystic, and the cysts are lined by all the elements of the skin—the epidermis, the dermis, and the dermal glands. Additional structures such as bone, cartilage, lymphoid tissue, and fat may be present. The cyst may be filled with sebaceous material produced by the glands in the wall.

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CHAPTER XII

CYSTS

A cyst is a collection of fluid in a rounded cavity surrounded by a definite wall or sac. Such localized collections of fluid are very common in the body. They form so heterogeneous a collection that it is difficult to combine them all under one common head, nor indeed is much to be gained by doing so. Moreover it is difficult in some cases to determine what should or should not be called a cyst.

Many cysts will be considered in detail when the organs in which they occur are discussed. Some of the more striking examples may be briefly considered in this place. We may divide cysts into the following groups.

1. Retention cysts.
2. Cysts of new formation; blood cysts.
3. Cysts of developmental origin.
4. Parasitic cysts.

RETENTION CYSTS

The blockage of the duct of a gland may be followed by cystic distension due to accumulation of the retained products. Such cysts are common in the breast and kidney, but the two important examples are the sebaceous cysts and the mucous cysts. Even in glands which have no external duct there may be cystic dilatation from excessive secretion on the part of the lining epithelial cells, as in the case of the thyroid.

Sebaceous Cysts.—A sebaceous cyst forms as the result of obstruction to the duct of a sebaceous gland either from dirt or inflammation. It is lined by several layers of flattened epithelium, these representing the secreting cells of the gland. The cyst contains sebaceous matter, a soft porridge-like material in which are found fatty granules and cholesterin crystals.

These cysts are commonest on the scalp and face, where they are frequently multiple, and although usually small they may attain the size of an orange. They also occur on the neck, shoulders, and back. The cyst forms a soft, doughy, globular swelling on the middle of which there may be a small black speck representing the closed duct. On the scalp the covering hair is often greatly thinned through pressure. As the cyst is situated in the substance of the skin the latter cannot be moved over it, thus contrasting with the dermoid cyst presently to be described.

The cyst may become inflamed and suppurate, or the overlying skin may ulcerate, giving rise to a condition which may closely resemble a malignant ulcer.

Mucous Cysts.—A mucous cyst has an origin similar to that of a sebaceous cyst, from obstruction to the duct of a gland in a mucous membrane. Not nearly so common as the sebaceous cyst, it appears as a small, tense, bluish mass, seldom attaining to any size, and containing clear mucinous fluid.

The commoner sites are the mucous surfaces of the lips, cheeks, tongue, and vulva. In the floor of the mouth under the tongue a mucous cyst constitutes the principal variety of *ranula*, which is a cyst of the sublingual gland, although occasionally the gland involved may be the submaxillary. It can be readily recognized from its bluish and somewhat translucent appearance.

CYSTS OF NEW FORMATION

Exudation of fluid from the blood vessels or lymphatics into a pre-existing cavity such as a bursa must not be regarded as a cyst. Similarly effusions of blood into a tumor or into a soft organ such as the brain are not to be included in this category. When, however, there is the formation of a new cyst wall about the fluid as well as an exudation of new fluid, the resulting condition may be called a true cyst.

Blood Cysts.—Of these exudation cysts the most important are the blood cysts. A hematoma in the subcutaneous tissues or a cerebral hemorrhage may, instead of being absorbed, undergo liquefaction and become surrounded by a very definite wall of fibrous tissue. Hematoidin crystals are present in the inner layers of the cyst wall, and the contents are a clear yellow fluid.

What are often called *blood cysts of bone* are not true cysts, but extravasations of blood into a myeloma or sarcoma, with consequent destruction of the tumor substance. There is no cyst wall.

Serous Cysts.—These cysts may commence as collections of fluid in the lymphatic spaces of the connective tissue in response to pressure, thus forming adventitious bursæ. A rare variety occurs in the mesentery, and may contain either serous or chylous fluid.

CYSTS OF DEVELOPMENTAL ORIGIN

The most important of these is the dermoid cyst, but the dentigerous cyst may also be mentioned; although it is not a true cyst, the condition known as cystic hygroma will be considered in this connection.

Dermoid Cysts.—The dermoid cyst of the ovary has already been described under the heading of teratoma (page 216). It is an entirely different condition from that under discussion, represents an attempt at the formation of a new individual, arises as a result of the abnormal development of an ovum, and to avoid confusion might well be called a dermoid tumor. Both conditions are called dermoid because of the

skin and its derivatives which form so prominent a feature in the cyst wall

Dermoid cysts are often termed *sequestration dermoids*, because they are formed by the inclusion of a rudiment of skin during the closure of one of the various embryonic clefts and fissures. They may arise from a vestigial epithelial-lined structure.

The cysts consist of a fibrous wall formed of cutis vera lined by stratified epidermis showing the normal papillary arrangement and containing hair follicles, sweat glands, and sebaceous glands. They contain sebaceous matter produced by the glands in the cyst wall. They are always congenital, but may increase in size during childhood, owing to continued secretion of the sebaceous contents. As the cyst is situated beneath the deep fascia the skin is freely movable over it.

The common position for dermoids is the angles of the orbit, especially the outer, and the upper eyelid. Occasionally they may occur in the scalp, the external ear, or the tongue. When overlying the skull the bone under the cyst is often defective, and the cyst may be connected with the dura mater by a pedicle. In the neck they may be in the middle line or situated laterally. The latter are called *branchial cysts*, since they arise from imperfect closure of a branchial cleft. The cyst may originate from the second cleft, in which case it is below and a little behind the angle of the jaw, or from the third cleft when it is on a level with the hyoid bone.

A curious form of dermoid is the *implantation dermoid*, arising from a fragment of skin which has been carried into the deeper tissues by a punctured wound. It rarely grows to any great size.

Dentigerous Cysts.—This is a loose term used to include a number of cysts of the jaws. Many names are given to the various cysts, but the simplest classification is (1) radicular cysts (80 per cent), (2) follicular cysts (20 per cent), and (3) multilocular cysts (under 0.1 per cent).

The *radicular cyst* develops from the epithelial sheath of Hertwig. Owing to the death of the tooth pulp there is a development of granulation tissue, with stimulation of the epithelial rest cells in the sheath of Hertwig. These cells undergo mucoid degeneration, so that a cavity lined by epithelium develops. The cyst formation is followed by a greater or less absorption of bone. The cyst is more common in the upper than the lower jaw, and most commonly affects the upper lateral incisors, and next the canines. Dorrance points out that the lateral incisor and canine are situated at the point where the intramaxillary process fuses with the maxillary process.

The *follicular cyst*, which, according to Bland-Sutton, is really a follicular odontome, arises from the tooth follicle. It occurs in the lower jaw, rarely in the upper, and contains a tooth, either a supernumerary one or one of the permanent set. In the latter case, which is the more common, the condition may be diagnosed by observing that one of the teeth, usually a molar, is missing. The cyst wall represents the expanded tooth follicle, and is of varying thickness. The expansion of

the bone may be so great as to give "eggshell crackling," and the fluid may amount to 2 oz. The cavity contains a viscid fluid, and the crown or the root of an imperfectly developed tooth.

The *multilocular cyst* is a rare form to which a variety of names has been applied. This is the epithelial odontome of Bland-Sutton. It is developed from the posterior end of the enamel ridge. The cyst contains many cavities, some of which communicate with one another. Malignant change occasionally occurs.

For further information regarding dentigerous cysts and odontomes the reader is referred to Bland-Sutton's "Tumors, Innocent and Malignant."

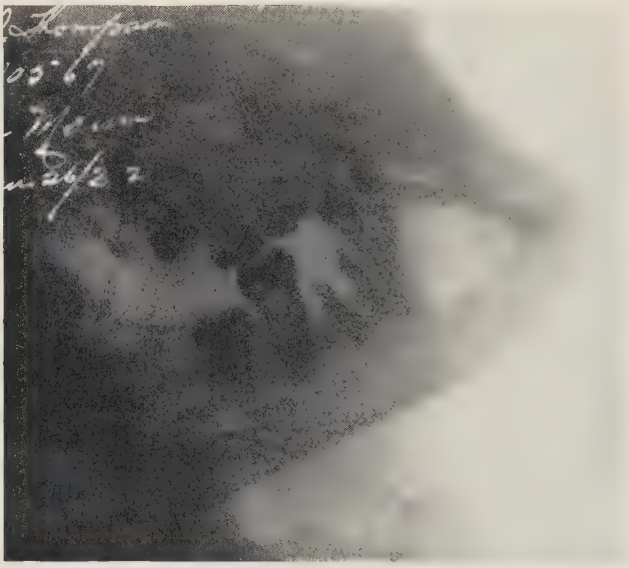

Fig. 66.—Dentigerous cyst of the lower jaw.

Cystic Hygroma.—There occurs in the neck a congenital cystic condition which, although really a tumor rather than a true cyst, may be referred to here. It is a cavernous lymphangioma, the spaces of which may be converted into veritable cysts, and is commonly called cystic hygroma of the neck. It may occur in the submaxillary region, in the posterior triangle of the neck, or in the axilla, where it forms a tense, painless swelling. It is liable to attacks of inflammation which may result in spontaneous shrinkage and cure. For that reason these masses are seldom met with after the age of puberty.

PARASITIC CYSTS

Hydatid Cysts.—The cystic stage of many parasites is passed in the lower animals, but in man the only one of any importance is the hydatid cyst. This is the larval or cystic stage of the Tenia echino-

coccus, a tapeworm which passes its adult life in the intestine of the dog. It is the smallest of all the tapeworms, measuring less than half an inch in length and possessing only three segments. The head is well armed with two rows of hooklets and four suckers.

The cycle of the tapeworm includes the carnivora and the herbivora. Starting in the intestine of the dog, the eggs are discharged in the feces, contaminate drinking water and green vegetables, and are ingested by man and such herbivora as sheep and cattle. In these animals the parasite passes through the cystic stage, but it can only return to the dog through that animal devouring the infected carcass or organs of an infected sheep or cow. The disease is confined to cattle-raising and sheep-raising countries, where the domestic relationship between men and their dogs is unusually close. Thus it is prevalent in Iceland, Australia, and South America in particular.

The ripe segments, crowded with ova, are discharged from the bowel of the dog, and ingested by one of the herbivora. The ova are surrounded by a capsule which becomes dissolved by the gastric juice, and the little embryos are set free. They are absorbed into the radicles of the portal vein, and are carried first to the liver. The liver, therefore, is the organ most commonly infected. If they pass the liver they will lodge in the lungs. Finally, if they pass the lungs they are carried into the systemic circulation and may settle in any organ of the body.

The embryo now develops into a cyst and enters upon the larval stage of its career. The cyst wall is formed of two layers, each of which is characteristic. The outer layer or *ectocyst* is thick and resembles coagulated white of egg; it is made up of a number of parallel layers like the leaves of a book. The inner layer or *endocyst* is the germinal layer. From it are budded off new heads or *scolices* of the tenia. Each scolex develops in a little cup-shaped process known as the *brood-capsule,* there being many scolices in each capsule. One germinal layer may give rise to very many scolices. In addition to forming new heads the endocyst may give rise to numerous daughter cysts, which usually develop within the main cyst, but sometimes outside of it. Within some of the daughter cysts new scolices may arise. Others remain sterile. The irritation of the cyst leads to the development of a well marked fibrous capsule from the organ in which it is situated.

The fluid in the cysts is clear and watery, non-albuminous, neutral, and of a specific gravity of about 1005. It often contains hooklets, and a precipitin reaction may be obtained when the fluid is mixed with the serum of a patient suffering from hydatid disease. Both of these points are of value in diagnosis. The laminated membrane is quite as characteristic as the hooklets. The blood displays a slight degree of eosinophilia, which may be of some diagnostic value. It never becomes marked, and is usually around 5 per cent. It is important to remember that if the cyst suppurates the eosinophilia disappears.

When the embryo dies the cyst ceases to enlarge, and secondary changes may occur. It may rupture externally, into a serous cavity, or into a hollow viscus; suppuration may occur with the formation of an abscess; or the cyst contents may become converted into a gelatinous mass and the wall become calcified. Leakage of the fluid may give rise to a rash resembling urticaria or scarlet fever, due to absorption of toxic products.

The commonest *site* of a hydatid cyst is the liver, then come the lungs, but it may occur in almost any part of the body, and the brain is by no means exempt. In the abdomen it is liable to be mistaken for other causes of enlargement, such as an ovarian cyst, and I have known the abdomen to be opened in search of a carcinoma, only to reveal a large hydatid cyst in the ileo-cecal region.

SPECIAL PATHOLOGY

CHAPTER XIII

NECK, SALIVARY GLANDS AND ESOPHAGUS

THE NECK

The chief diseases of the neck are inflammation, cysts and tumors.

Inflammation.—Inflammation in the neck deserves special consideration because of its tendency to become diffuse, and its relation to the deep cervical fascia. It spreads throughout the neck as a diffuse cellulitis, comparatively harmless when superficial to the cervical fascia, but fraught with the gravest consequences when deep to that structure.

Pus is formed in large amount, but being unable to escape it surrounds the great vessels and trachea, and may make its way into the mediastinum. It is under great pressure, so that the tissues feel hard and brawny. Respiration is interfered with through pressure on the trachea, and edema of the glottis is a common cause of death. To the severer forms of the condition the term *Ludwig's angina* is applied.

The disease usually occurs as a complication of one of the acute fevers such as scarlet fever or erysipelas, and the common infecting organism is the streptococcus pyogenes.

Localized inflammations due to the staphylococcus aureus are common at the back of the neck in the form of boils and carbuncles, owing to the constant irritation of the collar.

Tumors and Cysts.—Tumors and cysts may conveniently be considered together, for many of the cysts are cystic tumors. They may be mesial or lateral.

Mesial Cysts.—A mesial cyst or tumor arises from the vestigeal remains of the thyro-glossal tract, which passes from the foramen cecum at the base of the tongue to the isthmus of the thyroid gland. If the tumor is solid the structure is that of the thyroid gland, if cystic the cavity is lined by columnar epithelium. These masses are much commoner below than above the hyoid bone, but they may occur at the back of the tongue. They are firmly attached to the hyoid.

Lateral Cysts.—A lateral cyst or tumor may be a branchial cyst, a cystic lymphangioma, or one of the numerous varieties of cervical lymph gland enlargement which will be described in a subsequent chapter. Enlargements of the thyroid gland are also not considered in this connection.

A *branchial cyst* is derived from an unobliterated portion of, as a rule, the third branchial cleft, and is therefore situated at the level of the hyoid bone. In those cases in which it arises from the second

cleft, it lies just below the mastoid process and projects into the mouth. Although, of course, congenital they are often not noticed until puberty. The structure varies with the depth from the surface. When superficial they constitute a variety of dermoid, the cyst being lined by stratified epithelium and filled with sebaceous material. When deeper the lining epithelium is columnar and ciliated, and the contents more mucoid.

Occasionally the outer end of a branchial cleft may not be closed, giving rise to a *fistula* of varying depth. The external opening is situated at some point along the anterior border of the sterno-mastoid, commonly at the level of the angle of the jaw.

Cystic Lymphangioma.—This condition, known also as cystic hygroma and lymphatic cyst, has already been described in the chapter on Tumors. It is a not uncommon disease in children, but owing to its tendency to spontaneous cure it is seldom met with in the adult. The common position is the anterior triangle of the neck. It is more thin-walled and translucent than the branchial cyst.

Cervical Gland Enlargement.—This may be due, in order of frequency, to acute or chronic inflammation—from an inflamed tonsil, tooth, or septic focus in the jaw; tuberculosis; carcinoma of the lip, tongue, mouth, larynx or esophagus; syphilis in the secondary (rarely the primary) stage; Hodgkin's disease; and leukemia. The characters and differential diagnosis of the various conditions will be discussed when diseases of the lymphatic system are under consideration.

Cervical Rib.—This is not an uncommon condition. The accessory rib is attached to the transverse process of the seventh cervical vertebra, and may or may not be complete. It usually gives no trouble until the patient has grown up, when symptoms of pressure on the brachial plexus may occasionally develop, such as radiating pains down the arm and perhaps muscular atrophy.

Rare Conditions.—*Blood cysts*, beginning as a diverticulum of a large vein and later becoming isolated, may occur.

Cysts may arise in connection with the suprahyoid and thyrohyoid *bursæ*.

Tumors, either innocent such as lipoma (circumscribed or diffuse), fibroma, or osteoma, or malignant such as sarcoma or carcinoma, may occur primarily in the neck. A carcinoma may arise in the remnants of one of the branchial clefts.

THE SALIVARY GLANDS

The most important pathological conditions affecting the salivary gland are acute inflammation and tumors. The parotid is the common site of these disturbances, but the submaxillary and sublingual may on occasion be involved also.

Acute Inflammation.—Inflammation of the parotid may be non-suppurative or suppurative.

The *non-suppurative* form is known as *mumps*. The gland, usually in children, becomes acutely inflamed, hot, swollen, and tender, but

seeing that the condition is not due to pyogenic organisms, it ends by resolution, not by suppuration. An associated acute inflammation in the testicle is a fairly common complication, and in some cases this may be followed by atrophy of the testicle.

In the *suppurative* form the infection may come from the blood stream, as in acute fevers or in pyemia, or from the surrounding structures. Infection from the mouth by way of Stenson's duct is the most obvious and important method. The most frequent invaders are the staphylococcus aureus and the pneumococcus.

Suppuration usually occurs about the third or fourth day. Owing to the dense fascia which lies superficial to the gland the pus may extend upwards, downwards, or inwards (one variety of retropharyngeal abscess), but not to the surface.

Mixed Tumors.—Occurring chiefly in the parotid, but occasionally in the other salivary glands, in the buccal mucosa, and about the face, there is a group of tumors over which acute controversy has for long raged. While not uncommon in younger subjects, they are most frequently observed between the age of 20 and 40. Active growth is usually preceded by a period of quiescence, often many years in duration, during which a small nodule is noticed.

The *clinical course* varies greatly. In some cases the tumor grows steadily for two or three years, and then ceases to grow. In others growth extends over a period of many years until the tumor attains a great size, but even then, if encapsulated, it may be removed without recurrence. In still other cases the tumor possesses no capsule, invades the surrounding structures, and returns after removal. The lymph glands are seldom involved unless the tumor is interfered with, but unsuccessful removal may be followed by invasion of the cervical glands.

Structure.—The tumor, which is usually very firm in consistence, consists of a remarkable variety of structures. Indeed it is this complexity which has given rise to the corresponding variety of ideas regarding the nature of the growth.

The following are the principal structures, all of which may be found in any one specimen. (1) Broad or narrow strands of epithelial cells derived from the glandular alveoli and sometimes arranged in alveolar form. These cells may be flattened, and may line narrow channels like lymph spaces. This appearance is responsible for the prevalent idea that the tumor should be classed as an endothelioma. (2) Anastomosing cords of small dark epithelial cells with hyperchromatic nuclei. These cells are generally regarded as being those of a basal-cell carcinoma, and the arrangement is found in many small early tumors. (3) Mucoid connective tissue and cartilage are constantly present, sometimes in such excess that the tumor is taken for a myxoma or a chondroma. (4) Areas of lymphoid tissue are scattered throughout the stroma.

Nature of the Tumor.—As already indicated the most diverse views have been held as to the nature of the condition. Among these may be

mentioned the endothelioma theory, and the theory that, owing to the presence of both mesoblastic and epiblastic elements, the tumor must be of the nature of an embryoma, and thus derived from a germ cell.

The demonstration by Ehrlich that the mucin-secreting cells of the tumor could produce mucoid connective tissue from which eventually by a process of metaplasia cartilage may be formed, effectually cleared the ground. Difficult as it is to accept this view, as Ewing remarks, owing to its conflict with long-established theories as to tumor growth, yet it is impossible to avoid the conclusion that many of these tumors are simply adenocarcinomas with peculiar and exceptional metaplasia.

Ewing summarizes the position as follows:

"(1) The endothelial origin has been disproven.

"(2) No single source of the mixed tumors meets all the requirements. Some are distinctly adenomatous, and probably arise from the acini and ducts of the gland in which they are well incorporated. Others are encapsulated or extraglandular, and take the form of a basal-cell epithelioma. These probably arise from misplaced and occasionally embryonal portions of gland tissue. Branchial remnants may possibly be connected with this group.

"(3) The derivation of mucous tissue and cartilage from gland epithelium has been satisfactorily proven, and there is no necessity of including in the originating tissue any cartilaginous structures."

Calculi and cysts are conditions which do not call for detailed description here. The common site for a calculus is Stenson's duct, and one of the characteristic signs is that during meals saliva collects above the calculus, giving rise to a cystic swelling which gradually subsides. The common variety of cyst is the Ranula, which has already been described.

Rare Conditions.—The submaxillary and the sublingual glands may be the seat of inflammation or mixed tumors. Tuberculosis, actinomycosis, and syphilis may in rare cases attack any of the glands.

Mikulicz's disease is a very rare condition in which there is enlargement of the three salivary glands and the lachrymal gland. The pathology is unknown, the glands merely showing a dense infiltration with small round cells.

Primary *carcinoma* and *sarcoma* occur. Various innocent tumors such as fibroma, myxoma, chondroma, and angioma have been merely examples of the mixed tumor.

THE ESOPHAGUS

A patient who comes to a surgeon complaining of esophageal symptoms such as difficulty in swallowing and regurgitation of food may have a perfectly healthy esophagus pressed upon from without by a tumor or an aneurism. It is always wise to consider the possibility of aortic aneurism before passing a bougie down the esophagus.

If these outside conditions can be excluded the patient is suffering, in order of frequency, from (1) carcinoma, (2) stricture either cicatricial or spasmodic, or (3) an esophageal diverticulum.

Carcinoma.—Cancer of the esophagus, one of the most hopeless conditions with which the surgeon has to deal, resembles cancer of the tongue in that it occurs in about 80 per cent of cases in men over 40 years of age. In many cases raised white areas may be seen on the wall of the esophagus at some distance from the tumor, recalling the condition of leucoplakia.

The tumor does not begin at any random point of the tube, but at one of three definite sites: the upper end, the level of the bifurcation

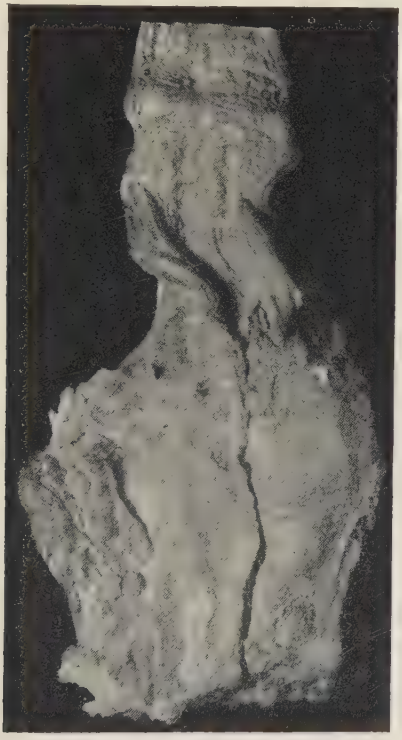

Fig. 67.—Carcinoma of esophagus with extreme stenosis.

of the trachea, and the lower end. As in the case of malignant disease in the stomach, the intestine, the gall bladder, and other situations, cancer of the esophagus may appear in one of three forms: (1) a flat infiltrating ulcer, (2) a more bulky polypoid mass, or (3) a diffuse infiltration. It commences in the mucous membrane as a squamous epithelioma, although in rare cases a columnar-celled carcinoma may arise from the mucous glands. Cornification is little if at all marked, and epithelial pearls are usually absent.

The disease slowly encircles the esophagus. It behaves like a true epithelioma in that it is locally destructive with involvement of the neighboring lymph glands, but without setting up metastases in distant organs. The glands involved depend upon the site of the cancer. If at the upper end of the esophagus the lower cervical glands will be enlarged, if in the middle or lower part a large mass of glands may be formed in the mediastinum which may give rise to very misleading physical signs and X-ray pictures. I have known a case demonstrated to a class of students by a physician of international fame as showing every sign and symptom of aortic aneurism—pulsating swelling in the chest, large X-ray shadow, inequality of the pupils, paralysis of the left recurrent laryngeal nerve, difficulty in swallowing, brassy cough, etc.—and yet at the post-mortem he was found to be suffering from cancer of the esophagus with a large mass of secondary glands in the mediastinum.

The earliest symptom is slight difficulty in swallowing, which may develop almost imperceptibly, together with loss of weight. As the cancer may invade any or all of the structures in the mediastinum, it is evident that the symptoms may be varied in the extreme. Death results within a space of twelve months.

Cicatricial Stricture.—The formation of scar tissue giving rise to stenosis is due generally to the swallowing of corrosive fluids, often taken for suicidal purposes, and occasionally to the laceration produced by impacted foreign bodies, such as a tooth-plate.

The destruction of the mucosa is naturally most marked at the narrowest points of the esophagus, so that the stricture generally occurs at the upper or lower ends. Dense scar tissue is formed which encircles the esophagus, but may extend for some distance up and down the tube, and by its contraction produces an extreme degree of stenosis.

In most of the hollow muscular tubes of the body partial (not complete) obstruction is followed by dilatation and hypertrophy of the part above, and collapse and atrophy of the part below. This is rarely seen in the esophagus. The probable reason is that the food collecting above the stricture is so easily ejected that dilatation of the tube has no time to occur.

Spasmodic Stricture or *Cardiospasm.*—This somewhat uncommon condition occurs in young men and women of neurotic temperament. For some reason at present unknown the muscle at the cardiac opening goes into such a forcible spasm that food is unable to pass. It is interesting to note that in this condition, in contrast to organic stricture, the lower part of the esophagus is often much dilated with hypertrophy of the wall.

Diverticula.—Diverticula of the esophagus may be divided into posterior and anterior varieties.

The *posterior* variety is the more common and important. It occurs at the junction of the esophagus and pharynx; indeed it is a pharyngeal rather than an esophageal diverticulum. It occurs most

frequently in men past middle life. As with other diverticula, hernias, and aneurisms, two etiological factors suggest themselves—weakness of the wall and increased pressure within. It has been the custom to suppose a congenital weakness of the pharyngeal wall, but for this there is absolutely no foundation. No case of diverticulum at this point has ever been met with in childhood. The important factor is probably prolonged abnormal intrapharyngeal tension. In some cases this may be due to organic stricture, but far more frequently it appears to arise from incoordinate action between the propulsive and sphincteric elements of the pharyngeal muscle. Gradually a protrusion of the mucous membrane of the lower part of the posterior wall of the pharynx occurs between the oblique and transverse fibers of the cricopharyngeus muscle. The forward displacement of the upper end of the esophagus still further directs the food back with ever increasing enlargement of the diverticulum. It projects downwards behind the esophagus as a sac into which passes much of the food, and which by its pressure on the esophagus may give rise to great difficulty in swallowing. The X-ray picture is highly characteristic.

The *anterior* variety occurs at the level of the bifurcation of the trachea. It is produced by the traction of fibrosing tuberculous glands which have become adherent to the esophagus, and is of little importance. The posterior form is a pulsion diverticulum, the anterior form a traction diverticulum.

Rare Conditions.—Syphilis, tuberculosis, or even typhoid fever may in rare cases produce ulceration of the mucous membrane of the esophagus, with the subsequent development of a stricture.

Various innocent tumors may occur, such as fibroma, myoma, lipoma, and warts. The fibroma is often pedunculated, and such polypi are found chiefly in the upper part of the esophagus.

Sarcoma is very rare. It may be round-celled or spindle-celled.

References for Further Study

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CHAPTER XIV

THE THYROID GLAND

Of the recent contributions which physiology has made to medicine none have been more notable or more far reaching in their results than the light thrown upon the nature and activities of the ductless glands. Such light is by no means clear and steady, but the darkness is no longer hopelessly impenetrable, and we are enabled to view the complex working of the human machine from a standpoint hitherto unattainable.

Disturbance of ductless glandular function is mainly of interest to the internist, but the thyroid, partly on acount of its ready accessibility, comes largely within the domain of the surgeon, and within recent years notable advances have been made in the surgical treatment of diseases of the gland.

Among those to whom our debt is greatest for their work in elucidating the complex problems of thyroid disease are McCarrison (epidemiology and etiology), Marine (experimental work), Wilson (pathology), and Plummer (symptomatology).

Development.—The thyroid gland is developed as a downgrowth from the ventral wall of the pharynx between the first and second pharyngeal pouches. The stalk connecting the embryonic thyroid with the pharynx becomes constricted to form the thyroglossal duct, which at birth is represented only by the foramen cecum, a dimple at the posterior part of the tongue which marks the site of the former opening of the duct.

Portions of the gland may become displaced during the course of development. A nodule occurring at the base of the tongue is called a *lingual thyroid.* Portions detached during the process of descent may form *accessory thyroids* in the neck. Finally, segments of the thyroglossal duct may fail to be obliterated, and may at any subsequent period give rise to *thyroglossal cysts* owing to the secreting power of the vestigial mucosa.

The *fetal thyroid* differs wholly in structure from that of the adult. At first it consists of an undifferentiated mass of embryonic cells, which later become arranged in tightly packed cords or masses, and are finally grouped around vesicles or acini. Even in the adult, however, solid masses of cells may be found in the interacinar parenchymatous tissue, the so-called "fetal rests," which give rise to the fetal adenomata.

On examining a fetal thyroid under a low magnification, and still more with the naked eye, one is at once struck with the remarkable degree of lobulation. The lobules are widely separated by an abundant connective tissue stroma. It is easy to understand how a new

formation of tissue from the embryonic cells during adult life should also display this character of encapsulation. An adenoma, therefore, will always be encapsulated.

In the fetal thyroid the interacinar parenchyma constitutes the greater part of the gland. Up to the age of puberty it remains fairly abundant, so that in young and adolescent patients enlargements of the thyroid frequently resemble the fetal type of structure. With advancing age the acini encroach more and more upon the interacinar tissue, till little of the latter remains. In addition to the glandular cells of the interacinar parenchyma, lymphocytes are also found in small numbers, but never in the masses which are frequently found in exophthalmic goiter.

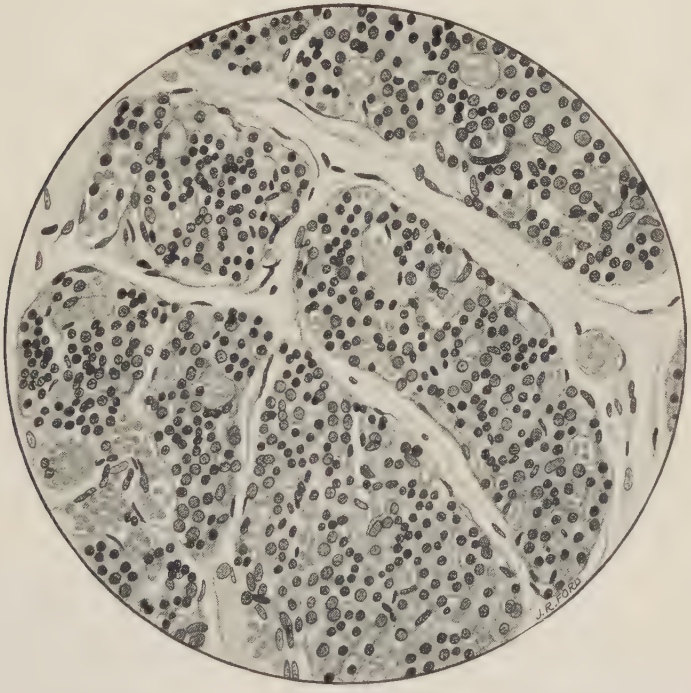

FIG. 68.—Fetal thyroid. The cells are arranged in solid lobules, with no attempt at the formation of acini.

The interacinar tissue varies then with different age periods rather than with differing states of glandular activity. The cells of this tissue are similar in form and probably in function to those lining the vesicles. It is likely that these interacinar cells act as a reserve from which the acini can draw a new lining, thus resembling the outer layer of cells of the acini of the breast.

Structure.—The thyroid gland is divided into a number of lobules by fibrous septa which pass from the connective tissue capsule, carrying with them the blood vessels and lymphatics with which the gland

is so abundantly supplied. The glandular parenchyma consists of closed acini filled with colloid, lined by epithelium, and separated by a varying amount of interacinar tissue.

The appearance of the vesicles varies in health with the state of activity of the gland. When the gland is in a quiescent or resting condition the alveoli are distended with dense colloid material which stains readily with aniline dyes. The lining cells are low cubical, or flattened, and the nucleus almost fills the cell. The vessels of the stroma are not congested. This colloid or quiet stage appears to be one in which iodine is being stored in the gland for future distribution to the body should sudden need arise, and it may be readily induced by feeding with iodine.

When glandular activity sets in the appearance of the vesicles at once alters. The epithelial cells elongate into high cubical or low columnar epithelium, the nucleus no longer fills the cell, the colloid is absorbed and replaced by fresh poorly staining fluid, and the vessels of the stroma become distended with blood.

Even in health, therefore, it is possible from a study of the histological picture to form a fairly accurate estimate of the activity of the gland. In disease, where the differences are more marked and striking, the same is true to an even greater extent.

Physiology.—The functions of the thyroid, with which the iodine content is intimately associated, can even yet hardly be defined in very precise language. It undoubtedly exerts a most potent and far-reaching influence over the various processes of body metabolism. Its secretion appears to act as a general and necessary stimulant without which there can be no health and vigor of the body, no flash and speed of the mind. "The thyroid gland is to the human body what the draught is to the fire; nay more, its iodine by its chemical interaction with certain unknown constituents of the cells is the match which kindles it." (McCarrison.)

It was in 1896 that Baumann first showed that the secretion of the thyroid contains a large amount of iodine in organic combination. Since that date much attention has been devoted to the iodine content of the thyroid, but it was not till 1914 that Kendall succeeded in isolating the active principle, an organic compound containing 65 per cent of iodine which he calls *thyroxin*, and which probably exists in the form of tri-iodo-tri-hydroxybeta-indol propionic acid. The administration of this substance even in the most minute quantities will produce the same series of phenomena as thyroid extract, and it has a remarkably rapid effect on myxedema and other conditions of thyroid insufficiency. Some one with a turn for the picturesque has remarked that thyroxin converts the sluggish toad into the lively frog.

GOITER

The thyroid is peculiar in that it is rarely affected by the four great causes of disease in other organs, inflammation, tuberculosis, syphilis,

and malignant disease. On the other hand it commonly presents a condition of enlargement, diffuse or localized, which may or may not be accompanied by symptoms of grave disturbance of general metabolism. To this condition the general name of goiter is applied.

Goiter is found throughout the animal kingdom from fishes to man. It is much more common in animals living under domestic conditions than in those in the wild state. This is particularly well seen in the case of the rat. Marine found that 90 per cent of the dogs brought to his laboratory in Cleveland (the center of a notably goitrous district) suffered from goiter.

The appearances found in goiter in man are very varied. On this account there has been a tendency to distinguish a large number of different types, to which different names are applied. Such terms as parenchymatous goiter, hyperplastic goiter, non-hyperplastic toxic goiter, toxic adenoma, cystic goiter, etc., may indicate much or little, but they tend to make the subject of goiter a very confused and perplexing one.

With a just appreciation, however, of the essential factors involved in thyroid hyperplasia we are now coming to regard the various forms as merely manifestations of one morbid process, bewildering in their complexity owing to the extreme sensitiveness of the thyroid to diverse stimuli, yet merely variations played upon one central theme, which may be detected running throughout the whole. More than half a century ago Virchow proclaimed the same truth. "With reference to true goiter the opinion has long been held that it comprises a series of definite varieties (struma lymphatica, cystica, ossea, vasculosa, etc.) which can develop independently of each other. This is wrong. All these so-called varieties are only different modes of development of essentially the same form of goiter."

Pathogenesis.—The thyroid, as already indicated, may be played on by a variety of stimuli, to which it reacts by hyperplasia either of the adult or the embryonic cells. It does not follow therefore, that it is necessary to look for one constant and invariable cause of goiter. In some cases it may be due to bacterial infection which possibly uses up the iodine necessary for the normal functioning of the gland, in others it may be due to deficiency of iodine in the food, in others to physiological stimuli such as puberty, menstruation, and pregnancy, in yet others to severe psychic shocks, as for instance in the cases of exophthalmic goiter which suddenly developed upon the bombardment of towns during the war. Even these last examples, however, may merely demand a greater iodine supply than is available.

The stimulus is followed by hyperplasia. When the stimulus is withdrawn the hyperplasia ceases, and the gland returns towards the normal. Such, for instance, is the thyroid enlargement of menstruation and pregnancy. Everything depends upon how far the hyperplasia has gone. If it is very slight the gland may return to normal. If it has proceeded further the best that can be done is a return to a resting stage in which the gland is permanently damaged, a

condition of colloid goiter. If the stimulus is continued the hyperplasia progresses indefinitely.

Although hyperplasia is associated with evidence of hyperfunction on the part of the thyroid, it does not follow that the essential cause of goiter is a stimulus applied directly to the thyroid. It may well be that goiter is merely a compensatory effort on the part of the thyroid to supply a demand on the part of the body. Our ignorance on the matter is profound, but from evidence to be discussed in relation to the iodine content of the thyroid it would appear as if it were in its essence a response on the part of the thyroid to the call of the tissues for iodine. This call may be due to an insufficient supply of iodine in the food or water, or to an undue demand because of abnormal physiological conditions.

The thyroid is an organ which reacts readily to stimuli, whether these be nervous, chemical, or bacterial. Being the organ with the largest relative blood supply in the body—it has been reckoned that its vascularity is five times as great as that of the kidney—it becomes swollen and congested at puberty, during menstruation and pregnancy, after the sexual act, etc. It has even been shown that temperature has an influence on the gland. If during the winter the weight of a series of thyroids from one species of animal is taken the average will be distinctly higher than that of a similar series taken during the summer. This, of course, is due to the increased metabolism of the winter months, and not to any direct action of cold on the thyroid itself. Such enlargement must be reckoned as physiological, but a slightly more potent or more prolonged stimulus may produce an enlargement which is no longer physiological but pathological.

Various influences may affect the thyroid, producing such a hypertrophy. Of these probably the most important is an infected water supply. Many striking examples of the relation of goiter to water supply are contained in the literature. At Bosel in Tarentaise out of a population of 1472 in 1848 there were 900 cases of goiter. The water supply happened to be changed, and 16 years later, the population being still approximately the same, the number of cases of goiter had dropped to 39. It has been noticed that the water in goitrous districts is particularly rich in bacteria. It is probable that it is not the action of the bacteria primarily on the gland which does the mischief, but rather the fact that they use up the supply of iodine in the water, the goiter thus being a compensatory phenomenon.

Among other observations, taken from the work of McCarrison and others, supporting the view that there is an intimate relationship between bacterial infection of water and the occurrence of goiter, the following may be mentioned.

When several villages in a goitrous district are situated along a mountain stream the prevalence of goiter shows a steady increase from above downwards.

Goiter can be produced in man by feeding with the residue on a Berkefeld filter left by goitrous water, although this property is destroyed by boiling.

Recent goiters in young subjects may be made to disappear by the administration of intestinal antiseptics, of which thymol is the most efficient.

It has been shown by Marine and Lenhardt that when fresh-water trout are kept in a series of tanks one above the other with a single water supply, the proportion of goiter increases from above downwards. Moreover the addition of pure water to each tank will prevent the onset of hyperplasia.

Gaylord has demonstrated that when such tanks are scraped and the residue dissolved in water, the administration of such water will produce goiter in the lower animals and in man. Boiling, as before, destroys this property.

When healthy animals (rats) are fed on fecal material from goitrous ones, goiter is produced.

Congenital goiter or cretinism may be produced by feeding a pregnant animal in a similar manner.

In all of these cases it is probable that the essential factor is the ultimate deficit in the iodine supply of the body.

The first response to the call is the appearance of those changes which we are accustomed to associate with increased physiological activity. These will continue, up to a certain limit, as long as the stimulus is kept up. When it is removed a period of regression will follow. Later again there may be another period of hyperplasia. The whole series of phenomena may be observed with great exactness in the experimental production of goiter in animals. A compensatory hyperplasia may be induced by the removal of a large part of the thyroid, whilst a condition of regression is brought about by the administration of iodine. Marine has shown that a hyperplastic thyroid may be made to return in this way to a fully resting condition in the short space of 3 weeks.

The following are the chief evidences of increased activity on the part of the thyroid.

1. Increased vascularity. The veins are enlarged, the capillaries lying between the acini are dilated, and the gland becomes red, swollen, and soft.

2. The epithelial cells lining the acini change from cubical to high columnar. They become increased in number, and projections or spurs appear within the acini, causing the latter to become irregular in outline and apparently smaller. In reality, however, they are enlarged. The nuclei show variations in size and in intensity of staining never seen in the normal gland, and indicating active cell-division. In young glands mitotic figures may be seen. This epithelial hyperplasia is the most important evidence of increased activity on the part of the thyroid.

3. There is an increase of the mitochondria in the acinar cells.

4. The cells of the interacinar parenchyma are increased, and many new alveoli are formed.

5. The fibrous stroma may become increased, and in Graves' disease may contain collections of lymphocytes.

6. The stored-up colloid is absorbed, and a thin, semi-fluid, poorly staining secretion is poured into the acini from the hyperactive epithelial cells.

7. The iodine content is low in inverse proportion to the hyperplasia.

The effect of the various hypertrophic and hyperplastic processes is to produce enlargement of the gland which is usually diffuse. It will be realized, however, that there may be considerable overactivity and hyperplasia as evidenced by disappearance of the colloid and a heightening of the epithelium with little or no enlargement of the gland as a whole. Hyperplasia, indeed is common, but goiter relatively rare.

The subsequent course of events depends upon whether or not the stimulus is continuous.

1. Should the stimulus cease to act, the hyperplastic condition gives place to a regressive or colloid state in which the thyroid returns more or less to its original condition, but bearing the indelible scars of its experience, and often remaining permanently enlarged. The vesicles become distended and filled with gelatinous colloid with a high iodine content, and the lining epithelium returns to a low cubical or it may be to a flattened form. The fire has burnt itself out, but evidence of the conflagration remains. The vesicles no longer present the uniform appearance as to size and shape characteristic of the normal thyroid. Some are greatly dilated, others small, and there project into the lumen spurs and processes, the vestiges of the previous hyperplasia. This is the condition to which the terms simple goiter and colloid goiter are applied.

The functional activity per unit volume of the gland is interfered with, but the general enlargement is usually sufficient to prevent symptoms of hypothyroidism from developing. Areas of hyperplastic tissue may remain in the intervesicular tissue, however, and these sometimes give rise to symptoms of glandular activity which it may be difficult to reconcile with an apparently colloid goiter.

In the event of the stimulus being repeated the whole cycle will again be passed through, but the resulting damage will be proportionately greater. Such a succession of intermittent stimuli is constantly seen in mountainous country where goiter is endemic, the exacerbations occurring in the springtime as a result of the heavy rains or melting snow at that season producing fecal contamination of the water supply. The hyperplasia in this case may be called a secondary hyperplasia. It differs from a primary hyperplasia in that the epithelial buds project into spaces which are unduly dilated and irregular, rather than into normal acini.

2. The stimulus may be continuous. The hyperplastic process is then continued without pause and without rest, the changes characteristic of that process are seen in an intense degree, and the symptoms of hyperthyroidism are continuous and marked.

No organ can endure excessive stimulation for an indefinite period without breaking down and degenerating. Accordingly in the course of time the lining cells undergo degeneration, become cast off, and fill the vesicles, and the connective tissue stroma is greatly increased. The volcano is dead. Enough glandular tissue may be left to provide a normal amount of secretion, or the destruction may be so great that a condition of hypothyroidism or myxedema is produced.

Such, in brief, is the series of phenomena which result from the action of a stimulus, either intermittent or continuous, upon the thyroid. The effect will naturally vary greatly in different cases, depending on the balance between the forces of hyperplasia and regression. At one pole we have the typical colloid goiter, with no symptoms apart from pressure, at the other is the equally typical Graves' disease. Between these, however, there are numerous intermediate conditions, more or less atypical.

Classification of Goiter.—Turning now to the actual problem of the classification of goiter we may recall that at birth and throughout life there are two varieties of cells in the thyroid. (1) Those which line the acini and which produce the characteristic secretion of the gland. (2) Those which are found here and there in the interstitial tissue between the acini and which may be regarded as fetal cells or cell rests. These parenchymatous interstitial cells are of great interest, and have not attracted the attention which they deserve. They closely resemble the cells which make up the fetal thyroid. Although not arranged in acini, it by no means follows that they are not capable of active function. The absence of acinar formation merely indicates that no provision has been made for storage. The thyroglobulin may still be produced, converted into thyroxin, and passed into the blood.

The multiplication of the fetal cells and the formation of acini gives rise to a localized enlargement which is known as an adenoma. Whether the term adenoma is a justifiable one is open to question. The mere fact that a hyperplasia is localized does not constitute it a neoplasm. Moreover the successful production of the characteristic secretion of the gland by the new tissue militates against this hypothesis.

Morbid changes may therefore affect either the fully formed acini or the interacinar collections of embryonic cells. The acini newly formed from the fetal cells are at first solid, later they acquire a lumen, and after a considerable time, it may be many years, they begin to make their presence felt by the production of symptoms of hyperthyroidism.

An ideal classification of goiter is not at present possible. We shall content ourselves with recognizing three forms: colloid goiter, adenomatous goiter, and exophthalmic goiter.

Colloid goiter and exophthalmic goiter are formed of adult cells. Adenomatous goiter, at least the fetal and possibly the colloid variety, is derived from the fetal cells. In the first two there is, or has been, overactivity of the cells of the preexisting acini. In the third there is a formation of new acini. These acini may be in no way hyperactive, but the increased bulk of actively functioning thyroid tissue may be sufficient to induce in time symptoms of hyperthyroidism.

We may conceive of *colloid goiter* as being the expression of a stimulus to the thyroid, acting only for a limited time. This stimulus is probably merely a chemical demand on the part of the tissues for an increased supply of thyroid secretion. As a result of the stimulus there is a slight degree of hyperplasia, dilatation of the acini, and therefore some enlargement of the gland. Upon the cessation of the stimulus, hyperplasia gives way to retrogression, and the dilated acini become filled with colloid, and lined by flattened epithelium. The dilated acini can never revert completely to the normal size, so that the gland remains permanently enlarged. It is normal physiologically but abnormal anatomically. If, during the period of hyperplasia the output of thyroxin is above the normal, there may be a mild degree of thyrotoxicosis, producing, naturally, only a slight increase of basal metabolism. In many cases there is not sufficient increase in the output to give rise to any symptoms. The difference between the two forms (toxic and non-toxic) is one of degree rather than of kind, and it is a mistake to consider them as separate forms of goiter.

Exophthalmic goiter, again, may be regarded as the expression of a much more intense stimulus acting for a considerable, but not an indefinite period. As long as it is acting, the gland is being whipped into feverish activity, and responds by hypertrophy and hyperplasia. When the stimulus is withdrawn, degeneration ensues, the hyperplastic acini again become filled with colloid, and only a few atrophic spurs projecting into their lumen like the withered branches of a burnt-out tree, remain as an indication of the fire which once raged so fiercely. Some specimens indicate this gradual transition in a very convincing manner. One part of the section may show quiescent dilated acini filled with colloid, and here and there a projecting spur, whilst in other parts the picture is still that of an active Graves' disease. Such an appearance is sometimes well seen after ligation of the superior thyroid arteries.

And what is the stimulus which produces this destructive activity? Is it again an urgent call from the tissues for help in maintaining their metabolic activity at an impossibly high level necessitated by the influence of some unknown agency, is it some bacterial toxin which acts directly upon the thyroid and goads it into a feverish activity which reacts upon the metabolism of the entire body, or is the thyroid disturbance to be attributed to some disorder which primarily affects the sympathetic nervous system? Many replies have been given to

these questions, but the existing state of our knowledge does not warrant a final and conclusive answer.

It can at least be said that Graves' disease is not a manifestation of pure hyperthyroidism. Some additional factor must be involved. It may be, as Kendall suggests, that there is a slight alteration in the structure of the thyroxin molecule, with a resulting toxic effect on the nervous system, and the production of the exophthalmos, the tremors, and the other nervous symptoms. Such a condition might well be called dysthyroidism rather than hyperthyroidism.

The *adenomatous form* is the most difficult to interpret. Here, for some unknown reason, the fetal cells awaken into activity, and in time may produce sufficient thyroxin to give rise to thyrotoxic symptoms. Once the new acini are formed they continue to function, so that the symptoms, although late in appearing, are of much longer duration than in Graves' disease. Here it is not a question of overactivity of the thyroid cells, but merely an increased bulk of normally functioning tissue which in time leads to symptoms of hyperthyroidism.

Iodine Content.—The thyroid differs from all other tissues of the body in that it contains iodine, and this element plays an essential part in the chemistry of thyroid function. The iodine content may be said to vary inversely with the degree of thyroid activity but directly with the colloid in the acini. An abundant iodine content indicates, therefore, that the gland is in a resting condition.

The iodine in food exists in a combined organic form, which cannot be utilized until it is split up, converted into sodium iodide, and presented as such to the thyroid. There is no advantage, therefore, in administering iodine in any form other than the iodide of sodium. The iodine in the blood (derived from the food) is being constantly built up into a non-toxic storage form, iodothyroglobulin, from the slow breaking down of which thyroxin is formed, and discharged into the blood in response to the demand of the tissues at a rate which under normal conditions gives rise to no toxic effects. In those words "in response to the demand of the tissues" we have the key to the complex changes which we are about to study.

Now the thyroid may be stimulated to undue activity in one of two ways. 1. There may be an insufficiency of iodine supplied to the thyroid. In this case the epithelium will undergo hyperplasia in its efforts to convert an unusual amount of iodothyroglobulin into thyroxin. The iodine content of the gland will fall. The administration of iodine will at once relieve the condition and restore the gland to a state of rest. 2. Owing to a heightening of metabolic activity there may be an undue demand for thyroxin. Again the response is shown by thyroid hyperplasia and a fall in the iodine content. Here also a more abundant supply of iodine may relieve the strain on the thyroid.

The analogy of the relation of the liver to carbohydrate function at once occurs to the mind. Glucose is stored in the liver in the inactive form of glycogen, being doled out in quantities sufficient to keep the blood sugar at the normal level. If the supply of sugar offered to

the liver falls too low, an abnormal amount of glycogen has to be converted into glucose. Exactly the same occurs if the demand of the tissues for sugar becomes too great. The thyroid may thus be regarded partly as a store, partly as a filter for iodine.

We have seen that the iodine supply to the thyroid may be insufficient. Indeed McCarrison goes so far in a recent paper as to class simple goiter as a deficiency disease. Now this deficiency may be actual. As a general rule we may say that goiter is prevalent in those districts which are removed from the sea and are at a high altitude. The iodides of the soil being more soluble than the chlorides, are the more readily carried away by streams, so that mountain soils are poor in iodine. But the deficiency may only be relative. McCarrison found that if rats were kept under hygienic conditions, or if they were put on a high fat diet, they developed goiter in spite of the fact that there was an abundant supply of iodine in the food. Under these circumstances the iodine was apparently not available for use by the thyroid; perhaps the gastrointestinal canal was unable to absorb it.

The behavior of the iodine content in abnormal thyroid conditions is of great interest and importance. The compensatory hyperplasia which follows the experimental removal of a considerable part of the thyroid is accompanied by a marked fall in the iodine content, the remaining portion being unable to deal with the increased demand of the tissues. The administration of iodine at once checks the hyperplasia, and the iodine content again rises to normal.

In *simple colloid goiter* Marine and his associates have demonstrated in a series of papers that iodine has a remarkable effect upon the thyroid. The gland shows a rapid and marked reduction in size, provided that other lesions such as adenomata are not present. The iodine appears to give the gland the needed rest, and thus enables it to return as near to the normal as may be consistent with the permanent damage which has already taken place. When hyperplasia has passed a certain stage, return to the normal is impossible. The best that can be hoped for is a colloid goiter. The amount of iodine necessary to maintain the thyroid in its normal resting state is about 1 mg. per gm. of dried thyroid. When the amount of iodine provided sinks below this level, hyperplastic change at once appear in the thyroid, only to be followed by involution when the amount of iodine in the gland again reaches the normal. It is the hyperplastic rather than the involutionary changes, which are checked by means of iodine.

Marine and Kimball have applied this knowledge to the prevention of colloid goiter in the school children in the goitrous district around Cleveland, and with startling success. They administered 2 gm. of sodium iodide in doses of 0.2 gm. over a period of 10 days twice a year to a large number of school children. Of 2,190 pupils taking the prophylactic dose, only five showed enlargement of the thyroid at the end of a year, whereas of 2,305 pupils not taking the dose, 495 showed distinct thyroid enlargement at the end of the same period. Of

1,182 pupils with thyroid enlargement who took the iodide, 773 showed a marked diminution in the size of the thyroid, while of 1,048 pupils who did not take the iodide, only 145 showed a similar diminution.

In *adenomatous goiter* the interstitial parenchymatous cells, the reserve cells of the thyroid, awaken into activity, and may or may not produce sufficient thyroxin to give rise to symptoms. Whether this awakening is due to a call on the part of the tissues, or to a stimulus acting on the gland we cannot say. Iodine administration is without effect on the adenoma, suggesting again that the adenomatous formation can not be regarded as a compensatory phenomenon.

In *exophthalmic goiter* the iodine content of the thyroid is very low. The administration of iodine, however, has no effect in checking the hyperplasia. It would again appear, therefore, that the hypertrophy is not simply a compensatory one. Sufficient iodine is supplied to the gland, but this is rapidly changed into iodothyroglobulin and thyroxin, so that little or none is stored in the thyroid.

In considering the effect of iodine administration in exophthalmic goiter a distinction must be drawn between iodine and sodium iodide. The use of sodium iodide is more likely to do harm than good, for it merely adds fuel to the already blazing fire. Iodine in the form of Lugol's solution on the other hand may have exactly the opposite effect, particularly on the basal metabolism. I have seen a case in which the basal metabolic rate was reduced by this means in 15 days from +96 to +47. It may be added that at this stage thyroidectomy was performed, and the metabolic rate at once resumed its former high level. The explanation is once more probably to be found in the intestinal antiseptic action of the iodine, whereby the injurious influences which are playing upon and stimulating the thyroid are removed.

Basal Metabolism.—The basal metabolic rate is the minimal heat production of an individual who has been at complete rest for at least 20 minutes, and who has taken no food for from 12 to 18 hours. It indicates the metabolism of the vital processes in the heart, lungs, glands, and nervous system, as distinct from the metabolism of muscular, digestive, and mental activity.

Although basal metabolism is naturally accelerated in such conditions as fever, yet there is only one condition in which the deviation from the normal becomes excessive, namely in hyperthyroidism. Basal metabolic estimations, therefore, are of great value in the diagnosis of the various forms of goiter, in forming a decision as to the most suitable time for operation—depending upon whether a case of Graves' disease is approaching or receding from a crisis—and in arriving at a conclusion as to the efficacy of the treatment employed.

The basal metabolic rate is invariably raised in the normal individual by the administration of thyroxin. In the hyperplastic stage of colloid goiter it may be slightly increased, but in the regressive stage it is normal or below normal. In adenoma with hyperthyroidism it is raised, but seldom above +35. In exophthalmic goiter the average

rate is +60, and in individual cases it may go as high as 100. In myxedema and cretinism it is well below normal.

Mitochondria. In 1916 there appeared a paper by E. Goetsch containing a study of the mitochondria in thyroid disease. These small, thread-like bodies are found in the cytoplasm of the cells of many organs, but are only visible in tissues which have been fixed in potassium bichromate and differentially stained. Goetsch found that there was an increase of the mitochondria in all hyperplastic thyroids. He further stated that in adenomatous goiter with thyrotoxic symptoms there was an increase in the mitochondria, even though other evidences of hyperplasia were absent, whereas in adenomatous goiter without toxic symptoms there was no such increase. Here, then, appear to be a valuable means of differentiation.

This work has been much quoted, but neither confirmed nor refuted. With this object W. Bolt, working in my laboratory, has examined a large number of goiters for the mitochondria content. He confirms the statement of Goetsch that hyperplasia is associated with a mitochondrial increase, but differs from him regarding the value of the test in adenomatous goiter. Briefly stated his conclusion was that every case in which there was an increase in mitochondria had already been judged to show signs of hyperplasia on other grounds. It was possible, therefore, always to arrive at a correct pathological diagnosis without resorting to the complicated method of staining for mitochondria.

Colloid Goiter

Simple colloid goiter is the goiter of adolescence. Like all other forms of goiter it is much commoner in women than in men. It usually appears between the ages of 15 and 20, frequently making its appearance about the time of puberty. As a rule it clears up in the course of a few years, and responds in a remarkable manner to the administration of iodine. The extremely important and successful work of Marine on the prevention of this form of goiter in school girls has already been referred to.

The hypertrophy is probably of a compensatory nature, and is due either to an undue call upon the thyroid for its active secretion, or to a deficient supply of iodine being offered to the gland. In either case, when an additional supply of iodine is administered the strain is taken off the gland, and the hyperplasia disappears. If adenomata are present they are not affected by the iodine (why should they be?), and are left standing out in sharp contrast to the rest of the gland. If the iodine is given prophylactically no hyperplasia will occur.

Morbid Anatomy.—The gland is uniformly and diffusely enlarged, thus presenting a marked distinction to adenomatous goiter. Its consistency is soft. On section the surface is uniform, amber in color, and presents a finely honey-combed appearance. The various degenerations, so common in the adenomata, are seldom seen in this variety.

The *microscopic appearance* resembles that of the normal thyroid. The acini, however, are more dilated, they vary much in size, and the lining epithelium is greatly flattened. The colloid is dense and deeply staining. The interstitial tissue is reduced to a minimum, and displays none of the parenchymatous cells found in the other forms of goiter, an important point which needs to be emphasized. Here and there traces of former activity may be detected in the form of atrophic spurs. Sometimes these spurs are composed of the tall epithelium so characteristic of active function. Many sections, however, may be examined without such an appearance being found.

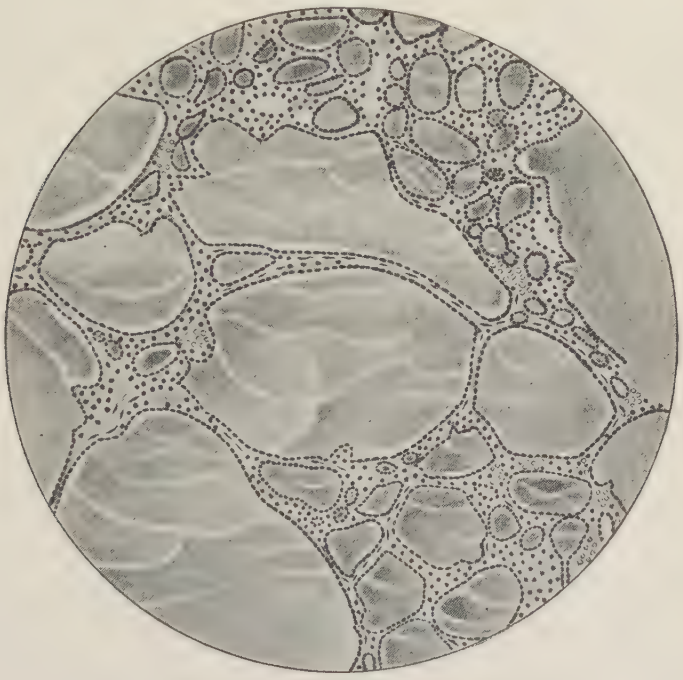

FIG. 69.—Diffuse colloid goiter. The acini vary much in size and are filled with dense colloid.

ADENOMATOUS GOITER

Proliferation of the interacinar parenchyma is of common occurrence between the ages of 15 and 25. The proliferation is usually localized, so that one or many nodular lumps are formed, which distort the normal smooth contour of the gland. The possession of a fibrous capsule is one of the most distinctive features of the adenomata, an appearance which is readily understood when the structure of the fetal thyroid is recalled. Occasionally the condition may be more diffuse, leading to a uniform enlargement of the gland, throughout which are scattered numerous small adenomata.

A considerable time elapses before the new acini, which are slowly formed, attain to active function, so that as a rule it is 10 or 15 years before symptoms of hyperthyroidism make their appearance. A toxic adenoma, therefore, seldom becomes toxic before the age of thirty. It may be stated as a general rule that thyrotoxic symptoms are 10 years later in their appearance than in the case of Graves' disease. Moreover the symptoms are much more gradual and insidious in their development, with none of the dramatic onset seen in exophthalmic goiter.

It is in this variety of goiter that hyperthyroidism is seen in its purest form. The manifestations are exactly those of long continued

Fig. 70.—Adenomatous goiter consisting of numerous colloid adenomata and one area of fetal adenoma.

administration of thyroid extract or thyroxin. Exophthalmic goiter, on the other hand, can never be reproduced in its entirety by such administration.

The brunt of the attack falls upon the cardiovascular system, whereas in Graves' disease it is the nervous system which is the principal sufferer. As the condition is usually a long-continued one, the circulatory system in course of time begins to display evidence of the

strain to which it has been subjected. The cardiac muscle degenerates, the heart dilates, and the arteries become sclerosed. A heightened blood pressure is the general rule.

Although many adenomata proclaim their presence by this train of toxic symptoms, it by no means follows that every adenoma is a toxic one. Many give rise to no general symptoms, but only to local evidence of pressure upon the trachea, the nerves, and occasionally the esophagus. It is the adenomata which, par excellence, are the cause of local trouble.

Adenomatous goiter does not present the same uniform picture as the other two forms. Two main varieties may be recognized, the fetal and the colloid. In their extreme forms these two are quite distinct, and can be recognized at a glance both naked eye and microscopically. After examining a large series of cases, however, and especially after a study of many sections from different parts of the same gland, the doubt arises as to whether we are really dealing with two different conditions, for intermediate grades can be traced which seem to point to a common origin. In some fetal adenomata areas are found which are typically colloid in appearance. In a colloid adenoma, on the other hand, there may be areas which cannot be distinguished from the fetal variety. The difference is frequently more marked in the gross than in the microscopic picture. It is probable, then, that both of these forms, arise from the fetal interacinar parenchyma.

Fetal Adenoma.—This form presents a sharply defined spherical mass, grey in color, elastic in consistency and of a peculiarly dense appearance which is quite unlike that of the translucent, honeycombed, colloid nodules. It is in this form of goiter that degenerations are most common. The grey surface may be flecked with specks of yellow, indicating necrotic areas. Hemorrhage into the loose interstitial tissue is of frequent occurrence, and may lead to sudden enlargement in the size of the goiter. The effused blood breaks down, and cyst formation may supervene. The fluid in the cyst is usually brown with blood pigment. In some cases it is clear and shimmering with cholesterin crystals. The cyst thus formed may attain to large dimensions and give rise to severe pressure symptoms. Fatty degeneration, hyaline degeneration, and actual calcification are all of common occurrence.

The *microscopic structure* is quite distinctive. No normal acini are to be seen. The tissue consists of a mass of very small, regular acini, lined by cubical cells, and containing a varying amount of colloid or none at all. The amount of the interstitial tissue varies greatly. In some cases the acini are closely packed together, giving an appearance of great density. Usually, however, they are widely separated by a loose, myxomatous-like stroma, giving the very opposite impression.

The colloid is not always confined to the acini. In some cases it appears to overflow the acinus and occupies the interstitial tissue. This phenomenon is difficult of explanation. It seems to occur particularly where there has been hemorrhage into the stroma. In

one specimen examined recently over half of the adenoma was of a deep red color, owing to the presence of abundant interacinar hemorrhage. The other half was quite pale. In the hemorrhagic part the space between the acini was flooded with colloid, whereas in the pale area the colloid was strictly confined to the acini. Iodothyroglobulin is soluble in normal saline solution, and it may be that the serum of the extravasated blood serves to wash the colloid from the acini into the surrounding tissue.

Although the commonly accepted signs of hyperplasia, such as tall columnar epithelium and the development of interacinar buds,

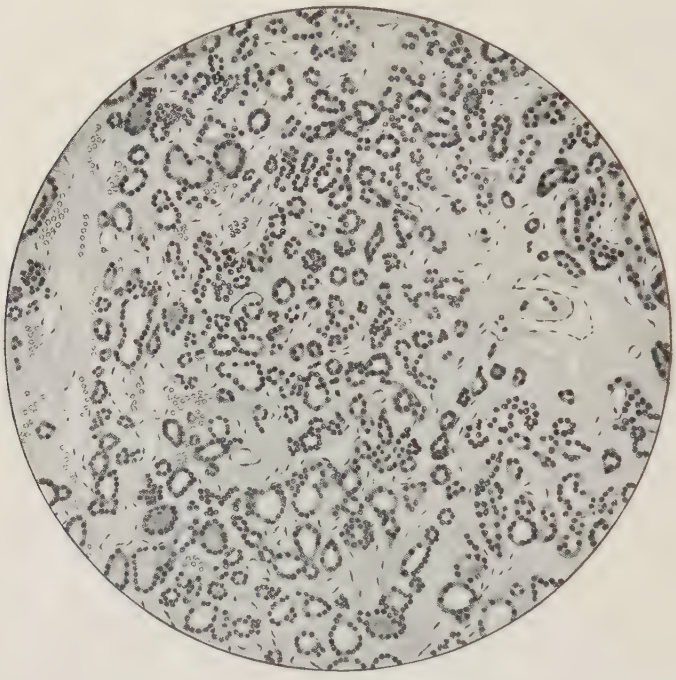

Fig. 71.—Fetal adenoma of thyroid. The numerous small acini are separated by an abundant stroma.

are usually absent, this is not always the case. Here and there distinct evidence of hyperplasia may be found. Such areas resemble islands of an exophthalmic goiter. It is stated that in some cases the greater part of the adenoma may present this appearance, but I have not encountered such specimens.

The entire mass is surrounded by the fibrous capsule which is characteristic of all adenomata. The acini of the adjacent portion of the thyroid may be much compressed by the adenoma.

Although this picture is not, as is sometimes stated, the same as that of the fetal thyroid—in the fetal gland there are solid masses of

cells in place of acini—yet there can be little doubt that the new acini have developed from the embryonic cells in the interstitial parenchyma. In a suitable section every stage of transition can be traced between a solid mass of cells and a fully formed acinus.

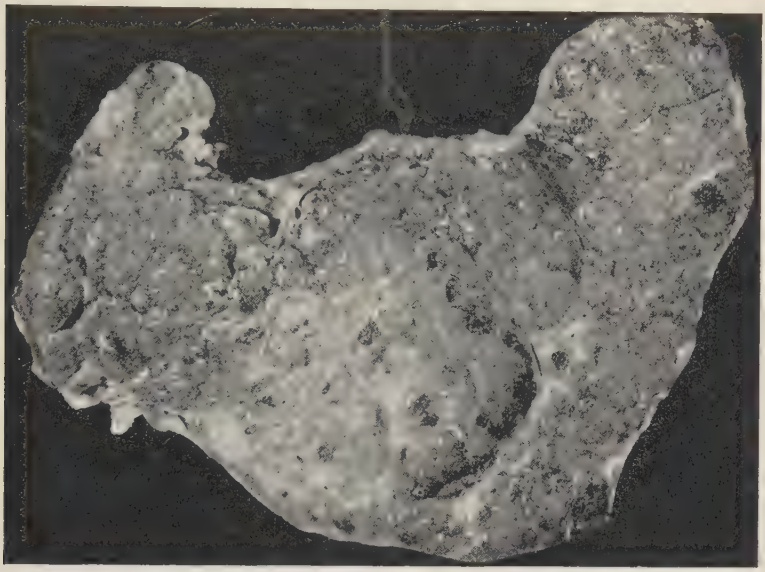

FIG. 72.—Thyroid showing multiple small colloid adenomata.

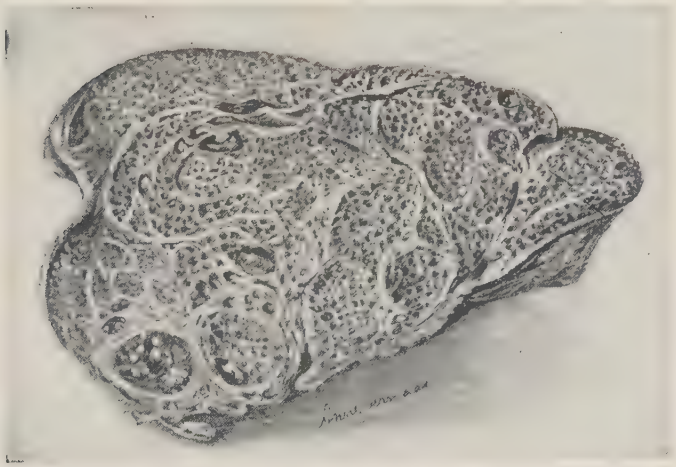

FIG. 73.—Colloid adenomata of thyroid.

Colloid Adenoma.—This form, which may be called adult adenoma, is of commoner occurrence. It takes the form of circumscribed masses of colloid material, similiar to that of the normal thyroid

or of colloid goiter. Each nodule is surrounded by a more or less well developed fibrous capsule. The nodules may be one or two inches in diameter, but frequently they are small and numerous.

Microscopically the nodule is composed of colloid-filled acini of varying size. It is difficult to say if these represent merely the original acini of the gland, or if they are really a new formation. The latter view is probably the correct one, for the impression gained from a study of many specimens is that the acini have been formed in the interstitial tissue. There are usually many acini of quite small size in addition to the more dilated ones. The epithelium is not flattened, but cubical, or may approach the columnar type. In places there may be projections into the acinar space indicating mild hyperplasia. The interstitial tissue often contains collections of parenchymatous cells which are not seen in typical diffuse colloid goiter. These cells are often quite large, with a large vesicular nucleus, and may resemble the cells of a large round-celled sarcoma. The appearance is one suggestive of active proliferation.

This form of goiter may be entirely non-toxic. In other cases it gives rise to symptoms of hyperthyroidism identical with those produced by the fetal adenoma. Both the fetal and the adult adenoma, therefore, may be toxic or non-toxic, depending entirely on the activity of the cells of the new tissue.

Diffuse Adenomatosis.—This is a condition described by Goetsch in which there is no formation of new acini, but rather a proliferation affecting the interacinar parenchymatous cells throughout the entire gland. There is no nodular formation, so that the term adenomatosis is a somewhat unfortunate one.

The thyroid is granular to the touch, but no definite nodules can be felt. Periglandular adhesions are common. The cut surface bleeds profusely. The consistency is not so firm as in exophthalmic goiter, nor does the gland present the characteristic lobulation seen in that condition.

Microscopically, there is a remarkable increase of the interstitial cells which are scattered diffusely throughout the gland. There is an associated atrophy of the colloid acini, with, in some places, an almost complete disappearance. The interstitial cells have no definite arrangement. Occasionally hyperplastic acini similiar to those seen in Graves' disease may be encountered.

The clinical symptoms are said to be those of mild hyperthyroidism, but with a normal basal metabolism.

The above description has been taken from the writings of Goetsch. I have had no personal experience with the condition.

Exophthalmic Goiter (Graves' Disease)

This disease is very much commoner in women than in men. It usually commences in early adult life, and the onset may be sudden and acute, or slow and insidious.

The cause of the disease is quite unknown, although apparently some irritant, bacterial or otherwise, acting continuously upon the thyroid. On the other hand the relation of the disease complex to the thyroid is by no means clear. The view commonly held is that the entire train of symptoms is due to overproduction of the internal secretion of the thyroid. But no one has succeeded in reproducing exophthalmic goiter by overfeeding with thyroid extract, although some of the symptoms such as nervousness or tachycardia may result.

The symptoms are essentially those of excitation of the sympathetic nervous system. In this excitation the thyroid, and probably some of the other glands of internal secretion, are involved, and no doubt some of the symptoms are due to excessive secretion on the part of these glands. The importance of the sympathetic in the pathogenesis of the disease has been further confirmed by Cannon's observation that when the phrenic nerve of the cat is anastomosed to the cervical sympathetic all the symptoms of exophthalmic goiter are reproduced, owing to the sympathetic being stimulated each time the animal takes a breath. It is only fair, however, to add that in a series of very carefully performed experiments Marine failed in every case to reproduce Cannon's results.

The four cardinal symptoms are enlargement of the thyroid, exophthalmos, tachycardia, and excitability of the nervous system as evidenced by tremors, etc. In addition the skin is moist and readily becomes flushed, the patient is very excitable and irritable, palpitation, diarrhea, and vomiting may occur, and peculiar eye symptoms are frequent. Loss of weight is a constant feature.

Perhaps the most important change is the enormously increased body metabolism, as indicated by calorimetric observations. It is as if some blast were blowing on the furnace of the body, fanning it into a condition of furious activity. There is no other disease condition in which a comparable increase occurs. As a result of the rapid nitrogen metabolism it is but natural that the patient should waste away, as if being burnt up. On the other hand carbohydrate metabolism is so interfered with that the sugar tolerance is lowered, the blood sugar is above normal, and glycosuria is apt to occur. This may be due to the inhibitory influence which the thyroid is known to exert on the pancreas, or possibly to the heightened activity of the sympathetic interfering with the storage of glycogen in the liver.

The course of the disease varies. The morbid process may be so acute that the patient dies of the disease itself, with symptoms of acute hyperthyroidism, cardiac dilatation, wasting and exhaustion. On the other hand the course may be more protracted, the intensity less acute, and the patient may ultimately recover or die of some intercurrent infection. Finally, the fire may burn itself out, the thyroid breaks down under the constant stimulus, degenerative changes follow, and a partial condition of myxedema or thyroid insufficiency may

develop. Speaking generally it may be said that the symptoms of exophthalmic goiter are more acute in their onset than those of the

FIG. 74.—Exophthalmic goiter. Moderate enlargement of the gland.

hyperthyroidism of a toxic adenoma, but that at the same time they are more self-limited. It must be remembered, however, that by the

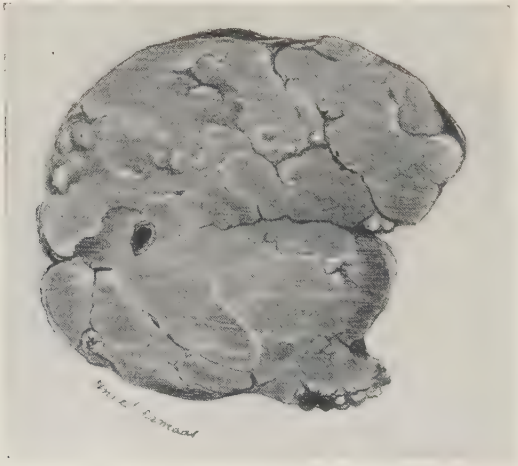

FIG. 75.—Exophthalmic goiter.

time the thyroid has ceased hyperfunctioning, many of the vital organs of the body, particularly the heart, have been permanently damaged,

and the patient is merely a wreck, and a permanent wreck, of her former self.

The thyroid is usually enlarged, but this is not always the case. The enlargement is as a rule uniform, but one lobe may be more involved than the other. The surface is covered by enormously distended veins, which obtrude themselves on the notice of the operating surgeon.

The **gross appearance** of the gland is quite different from that seen in colloid or adenomatous goiter, and in typical cases the two can be distinguished at a glance. It is firm in consistence, of a dense, opaque,

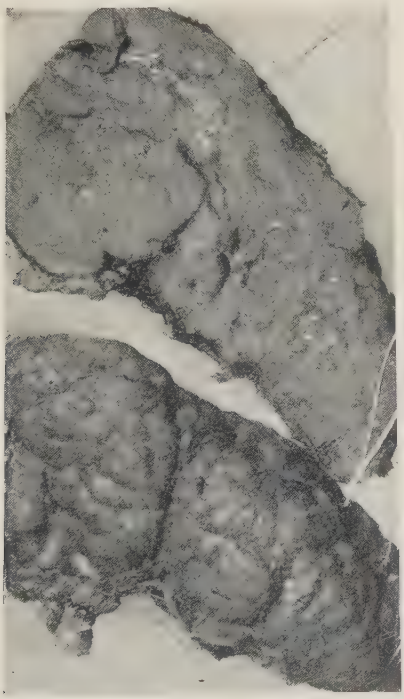

FIG. 76.—Thyroid: exophthalmic goiter. The cut surface resembles the pancreas in texture.

meaty appearance, very different from the translucent look of the colloid goiter, and the evident lobulation which it presents at once suggests a resemblance to a salivary gland or to the pancreas.

The **microscopic picture** is equally characteristic and distinct. It is one of hyperplasia and great glandular activity. The vessels are greatly dilated. The epithelium is tall and columnar, and many of the nuclei display that irregularity in size and abnormal staining qualities which are suggestive of rapid multiplication. There is marked epithelial hyperplasia, with a resulting infolding and projection of the lining into the alveoli. The latter, therefore, although in reality

larger, appear smaller than normal, and they no longer contain colloid, but only the thin poorly staining secretion poured out by the hyperactive epithelial cells. In many places the acinar lumen is completely obliterated, and nothing can be seen but a dense mass of epithelial cells. The microscopic as well as the gross appearance not infrequently recalls that of a secreting gland.

The intervesicular parenchyma is also said to show evidence of hyperplasia, and small newly formed alveoli are described. It is difficult, however, to convince oneself that such is the case, for the epithelial proliferation is so great that the interacinar stroma can often not be distinguished with certainty. In addition to the greatly

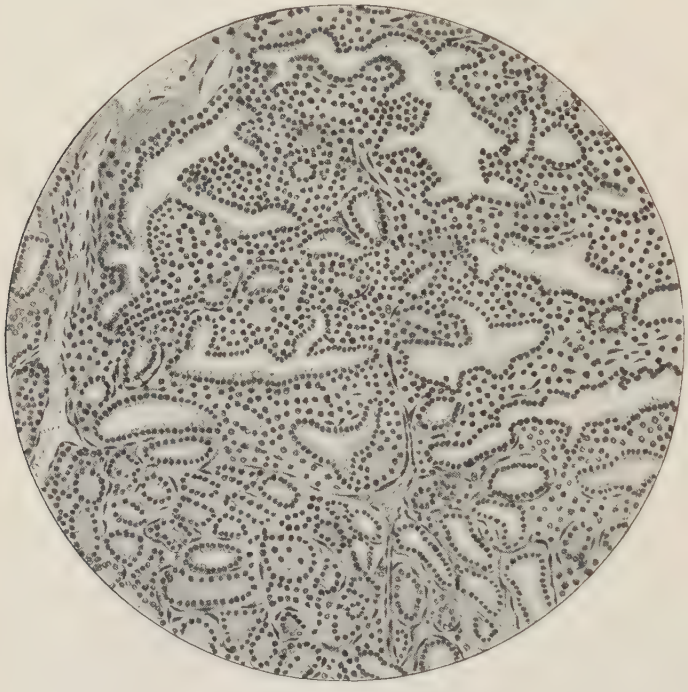

Fig. 77.—Exophthalmic goiter, showing a marked degree of epithelial hyperplasia.

increased vascularity, the stroma shows definite collections of lymphoid cells which are highly characteristic of the condition. The occurrence of these dense lymphoid areas is certainly a matter for surprise. They may owe their origin to the action of the original irritant which is exciting the gland to overactivity, or they may, in common with the lymphoid hyperplasia elsewhere, be merely an inexplicable result of the general condition of hyperthyroidism. In this connection it is of interest to note that Cameron (University of Manitoba) has recently shown that when rats are fed on thyroid tissue there results a general overgrowth of lymphoid tissue throughout the body. These

lymphoid nodules are not found in other forms of goiter. They form, however, a prominent part of the microscopic picture in the thyroid in myxedema, suggesting that the myxedema has been preceded by a period of hyperthyroidism.

Changes in Other Organs.—The changes in the thyroid are the most striking, and therefore have received the largest share of attention. Many other tissues, however, show more or less constant changes in Graves' disease. To what extent these are merely effects of the thyrotoxicosis, or to what degree they play a primary part in the pathology of the condition it is not at present possible to say.

The *lymphoid tissue* shows changes almost as constant in character as those of the thyroid itself. There is a general lymphoid hyperplasia. The thymus is said to be very frequently enlarged, although in my own experience this is by no means a constant change. The tonsils, the Peyer's patches in the small intestine, the solitary glands in the large intestine, and the Malpighian bodies of the spleen show a hyperplasia similar to that of status lymphaticus. There is often a relative lymphocytosis in the blood ranging from 25 to 60 per cent.

The *blood*, in addition to the lymphocytosis, shows a mild degree of secondary anemia, and a decrease in the total number of leucocytes, a diminution which is effected at the expense of the polymorphonuclears.

The *heart* is enlarged. The ventricles are dilated, and their walls are hypertrophied. In cases of long standing there may be degeneration of the myocardium associated with fibrosis. An important contribution to the subject has recently been made by Hashimoto. As a result of feeding rats on thyroid extract he found not only enlargement of the heart, but also curious collections of cells between the muscle fibers and around the blood vessels, indicating the presence of a chronic non-suppurative interstitial myocarditis. Many of these cells are peculiar, large, pale cells very similar to those of the Aschoff bodies seen in the heart in acute articular rheumatism. In addition there are lymphocytes and fibroblasts. Somewhat similar lesions have been described by Fahr as occurring in goiter hearts in the human subject. In a series of 6 rats fed upon thyroid by Professor Cameron of the Biochemistry Department, University of Manitoba, I was unable to verify the findings of Hashimoto.

The *muscles* show in places fatty degeneration. This is particularly well marked in the quadriceps extensor, and no doubt accounts for the difficulty the patient has in raising his foot to a height.

The *nervous system* changes are probably of great importance. Wilson has demonstrated degenerative changes in the cervical sympathetic ganglia in the large majority of a small series of cases. The principal changes are excessive pigmentation of the nerve cells, chromatolysis, and finally atrophy. In view of the relation of the sympathetic system to the thyroid and to the symptoms of Graves' disease, these findings are of great interest.

TABLE ILLUSTRATING SOME CHARACTERISTICS OF THE VARIOUS TYPES OF GOITER

	Colloid goiter	Adenomatous goiter	Exophthalmic goiter
Age	Adolescence.	Goiter develops 15–20. Symptoms develop over 30.	20–35.
Onset of symptoms		Gradual.	Sudden.
Toxic symptoms	Seldom and slight.	In over 20 per cent. Cardiovascular. Continuous.	Always. Mainly nervous. Exacerbations.
Systolic blood pressure	Normal.	High in toxic cases.	Normal.
Basal metabolism	Around normal.	Seldom over +35.	Average of +60.
Distribution	Diffuse.	Nodular.	Diffuse.
Hyperplasia	Only in earliest stages.	Sometimes.	Always.
Mitochondria	Absent.	Present in toxic cases.	Present.
Colloid	Abundant.	Variable.	Scanty or absent.
Iodine content	High except in early stage.	Normal.	Low.
Response to iodine	Marked.	None.	None.
Degenerations	Rare.	Very common.	None.

MYXEDEMA AND CRETINISM

So far only conditions of thyroid enlargement, with or without toxic symptoms, have been considered. There remains to be considered a peculiar train of symptoms now recognized to be indicative of thyroid insufficiency.

Cretinism.—The thyroid may become hypoactive at any period of life. When it does so *in utero* the child is born a cretin. Cretinism may be endemic or sporadic. Both forms are congenital, due to the action of injurious influences on the thyroid during fetal life.

Endemic cretinism occurs in districts, such as the Alps and Himalayas, where goiter is endemic. According to McCarrison 96 per cent of the mothers of cretins in endemic districts suffer from goiter. Although the disease is undoubtedly due to goitrigenous influences acting on the fetal thyroid, yet the cretin rarely manifests a goiter at birth. By the age of three, however, he has often developed one, and by ten he is usually goitrous. The explanation of this peculiarity is not clear, but apparently the few remnants left of the gland are so modified as to be unduly susceptible to goitrous influences encountered in the endemic district, and develop into a goiter. If the child be removed from the district a goiter will usually be prevented.

The sporadic form may occur anywhere and may be due to deleterious influences, other than those which produce goiter, acting on the embryonic thyroid. Goiter is rare in this form of cretinism, but may occur.

The cretin, like Peter Pan, is a boy who never grows up. He remains a dwarf physically and mentally. The mind, the skeleton, and the sexual organs do not develop. A "sad, old child" is a description as true as it is pathetic. The stature is stunted, the

head large, the face broad, the features coarse, the arms short and curved, the sexual organs undeveloped, and the mental powers little better than those of an imbecile. The thyroid is converted into a mass of fibrous tissue.

The striking skeletal changes are due to defective development of those bones which develop in cartilage. Membranous bones, such as the clavicle and the vault of the skull are comparatively normal, but cartilage bones—the long bones and the base of the skull—show extreme retardation of growth.

Myxedema.—This is the condition produced by thyroid insufficiency in the adult. The symptoms are similar to those of cretinism, and are the very antithesis of those of Graves' disease. All the processes, both mental and physical, are slowed, the fire burns low, the basal metabolism, as shown by the calorimeter is much below normal.

The patient, usually a woman, is heavy, obese, intensely phlegmatic, and will sit for hours without moving. There is a curious similarity in the facial expression, or lack of expression, of all such patients. A typical case can be recognized at a glance. The face is broad, the features coarse, like those of an Esquimo. A malar flush is common. The skin is rough, dry and wrinkled, and the patient is very sensitive to the cold. A premature baldness is characteristic, not commencing in the usual situation, however, but choosing the frontal region and the nape of the neck—the "cassowary neck." An early sign of diagnostic value is the falling out of the hair of the outer third of the eyebrow.

The most characteristic change to which the disease owes its name is an infiltration of the skin and mucous membranes with a mucus-like substance, producing a kind of pseudo-edema which, however, does not show pitting on pressure. This infiltration may involve the entire skin, but is most marked in the face, neck, supra-clavicular fossæ where characteristic pads are formed, and on the backs of the hands. The hand is broad, fat, and clumsy, "spade-like" in appearance.

The mucous membranes suffer likewise from this process of infiltration, so that there is swelling and impairment of function in the conjunctivæ, nose, mouth, larynx, bronchi, gastro-intestinal tract, and genito-urinary system. The tongue is so thick and swollen that it may protrude from the mouth.

The thyroid, in the most advanced cases, is atrophic, hard, and converted into a mass of fibrous tissue with complete disappearance of the parenchymatous tissue. Scattered throughout it, as in our solitary autopsy case, there may be well defined nodules of lymphoid tissue, strongly reminiscent of the similar condition in Graves' disease. The significance of these nodules is not certain, but they suggest that the myxedema has been preceded by a period of mild hyperplasia. It is seldom that advanced cases are encountered nowadays, owing to improved diagnosis, and the most efficient of all medical treatment. In the event of a mild case coming to autopsy the degree of atrophy will be correspondingly moderate, and although portions of the gland

Fig. 78.—Myxedema. Thyroid atrophied and extremely dense.

Fig. 79.—Myxedema. The normal thyroid structure is almost entirely replaced by dense fibrous tissue and collections of round cells.

may be fibrosed, enough parenchymatous tissue remains to allow of the glandular activity being carried on at a low level.

The pituitary gland often shows some enlargement, with excess of colloid material in the pars intermedia. It has been suggested that this is a compensatory hypertrophy on the part of the pituitary to atone for the thyroid deficiency. Of this there is no proof. The change may equally well be due to the effect of the same influences which have been acting on the thyroid, and it is the part of wisdom not to be carried away by the speculations of the endocrinologists.

The cause of myxedema is insufficiency of the thyroid, but as to the factors which produce such insufficiency we are still largely in the dark. In a consideration of the cycle of activity through which the thyroid may pass it has already been shown that a period of hyperactivity may be followed by one of hypoactivity, that the hyperplastic thyroid tends eventually to degeneration and atrophy. While, however, it is true that symptoms of minor thyroid insufficiency may accompany or follow goiter, yet myxedema is not especially common in goitrous districts, and the classical examples of the disease are not associated with goiter.

It would appear, therefore, that the condition must be caused by injurious influences, other than those which produce goiter, acting upon the thyroid. The effect of heredity is marked, for a woman with myxedema is very liable to give birth to a child with impaired thyroid function.

Cachexia strumipriva is a term applied to the effects occasionally produced by operative removal of a goiter (struma). Total removal of the gland may produce symptoms similar to those of myxedema, but with wasting as the most marked feature. Somewhat similar results have been obtained in animals. The condition is, however, a very rare one, and with modern surgical methods is almost never seen.

INFLAMMATION

It is but natural that such a highly specialized gland as the thyroid with so abundant a blood supply should be involved in general inflammatory processes. It is seldom that the inflammation thus induced attains to any marked degree. If, however, general conditions predisposing to thyroid degeneration, such as chronic malnutrition, be present, symptoms of thyroid insufficiency may subsequently develop which may be traced to the previous injury thus received.

A mild form of thyroiditis may be present in many infections, but more especially in acute tonsillitis and acute articular rheumatism. A severe attack of typhoid fever, which leaves its marks on so many tissues, may damage the thyroid to a considerable degree. The gland is often somewhat enlarged and tender in secondary syphilis, so that in some countries this is regarded as an indication of importance.

In exceptional cases suppuration may develop, the gland becomes swollen and inflamed, and an abscess forms. This may discharge into the mediastinum, or into the larynx, trachea, or esophagus. If

recovery occurs the usual scarring will result, with frequent deposition of lime salts.

The effect on the thyroid of a general intoxication is always more marked when the gland is already diseased, even though it may be in a quiescent state. Thus in one case of Graves' disease which came under my observation there had been no symptoms of hyperthyroidism for four years, but an attack of epidemic encephalitis resulted in a return of all the symptoms.

WOODY THYROIDITIS

A rare but important form of chronic inflammation is that to which the names of woody thyroiditis and iron-hard thyroiditis have

FIG. 80.—Tuberculosis of the thyroid.

been applied. It is of importance because of its liability to be mistaken for carcinoma. The gland enlarges rapidly, and is found at operation to present a remarkable appearance. The enlargement is uniform and involves the whole gland, the surface is smooth, the color whitish, the limits are poorly defined as the gland appears to merge with the surrounding tissues to which it is firmly adherent, and is of an extraordinarily hard consistence so as fully to deserve its name of woody or iron-like. In the only case which I have seen it was thought that the specimen must have been preserved in pure formalin before reaching the laboratory.

Microscopically it consists of dense sclerotic tissue in which only remnants of the glandular tissue remain. The peculiar fibrosis recalls that of the somewhat similar condition described in the pancreas by Riedel, and in the submaxillary gland by Michalies.

In many cases no cause can be discovered. In our case areas of tuberculosis were scattered throughout the gland, and tuberculosis is probably the most important causal factor.

The principal symptoms are rapid enlargement of the thyroid, local pain and tenderness, and marked dyspnea. Although closely resembling carcinoma, it differs in that it usually occurs under the age of forty, as a rule the gland has not previously been the seat of goiter, and the surface is not nodular as in carcinoma.

CARCINOMA

Cancer of the thyroid presents some unique features, which make it a condition of great theoretical interest. Although it may arise in an apparently normal thyroid it usually develops in one already the seat of goiter, thus exemplifying the general rule that carcinoma does not develop in normal tissue, but in tissue that has been previously injured.

Its most peculiar feature is its tendency to set up secondary growths throughout the skeleton, a characteristic which it shares with the prostate and with the breast. These growths occur especially in the skull, the pelvis, the sternum, the ribs, and the long bones.

The secondary growth is remarkable for the manner in which it reproduces, not the structure of the primary cancer, but that of the normal thyroid. Moreover, this new-formed thyroid tissue is apparently able to functionate in a useful manner, thus differing from all other forms of malignant overgrowth. Cases are on record in which a malignant thyroid has been removed without the production of symptoms. When, however, a metastasis was removed at a later operation marked symptoms of myxedema soon made their appearance.

The primary condition in the thyroid may be either a carcinoma simplex or an adenocarcinoma. In the latter case the alveoli may resemble those of the normal thyroid in a remarkable degree. The tumor forms a hard nodular mass, from the surface of which "cancer juice" can often be expressed, often showing areas of softening in the center, and firmly adherent to surrounding parts.

Most extraordinary are those cases in which, although multiple secondary growths showing typical thyroid structure are present throughout the skeleton, yet the gland itself shows merely the enlargement of a colloid goiter. The condition is known as general thyroid malignancy. No adequate explanation of this phenomenon has been given, but it is possible that a small carcinomatous nodule which was overlooked may have been present in the thyroid.

For a very full discussion of carcinoma of the thyoid the recent paper of Wilson should be consulted, containing a summary of the data

on 290 patients with malignant tumors of the thyroid, with a most extensive bibliography

RARE CONDITIONS

Sarcoma may occur, may be of any of the ordinary varieties, and presents the usual characteristics.

Tuberculosis is perhaps more frequent than has usually been supposed. Both the miliary and caseous forms may occur. Many cases of woody thyroiditis are tuberculous in nature.

Syphilis.—Although secondary involvement is common, tertiary lesions such as gummata are very rare.

Cysts.—Echinococcus cysts have been reported.

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CHAPTER XV

LIPS, MOUTH, AND TONGUE

THE LIPS

The common pathological appearances in the lips are (1) fissures or cracks, (2) scars, (3) an indurated nodule which may be ulcerated.

Fissures.—The somewhat painful condition called "cracked lip" is of common occurrence in young people in cold weather.

Any other fissure is most probably *syphilitic*. A syphilitic fissure may be distinguished from the preceding condition by the red infiltration which surrounds it, and by the fact that when the lip is everted a mucous patch may be found on the inside corresponding to the fissure. Such fissures are commonest at the angles of the mouth.

Scars.—The presence of white, stellate scars at the angles of the mouth is strong presumptive evidence of a previous attack of syphilis, and especially of congenital syphilis. The scars represent the site of healed fissures.

An indurated nodule, which may or may not be ulcerated, is probably either an epithelioma or a primary chancre. If on the lower lip the condition is likely to be epithelioma, although a chancre may also occur there. If on the upper lip it is almost certain to be syphilitic.

Epithelioma.—Epithelioma of the lip is the commonest form of malignant disease of the face, and accounts for 2 per cent of all deaths from cancer. It is at least 20 times commoner in the lower than in the upper lip. Moreover it is much more frequent in men than in women; most of the figures attribute only from 2 to 5 per cent of the cases to women. It has long been taught that the habit of pipe-smoking is sufficient to explain this difference, but Broders' recent work has shown that this belief is without foundation, for he found relatively little difference in the frequency in smokers and non-smokers.

The general rule that cancer does not originate in an absolutely healthy tissue holds true in the case of the lip, for it is frequent to find an antecedent history of a cracked or fissured lip, an abrasion due to the chronic irritation produced by a jagged tooth, or even the trauma associated with playing the flute or the bugle. Any lesion which breaks the protective covering of epithelium, such, for instance, as a crack, or a patch of seborrhea or leukoplakia, may be the precursor of epithelioma.

The disease begins as a flat nodule or an indurated crack at the junction of the skin and mucous membrane. If the growth extends towards the surface an ulcerated, fungating, warty mass is formed. If towards the deeper structures an indurated nodule is the result, which

only becomes ulcerated later. The ulcer presents the hard, raised edges characteristic of malignancy. As the ulcer spreads it may destroy the lip and the tissues covering the chin, and may finally involve the mandible. The disease, if not treated, usually terminates fatally in from two to five years. Removal of the tumor and of the infected glands results in cure in 70 per cent of cases. The reader is referred to Broders' work on the varying grades of malignancy, an account of which will be found on page 195.

Like epithelioma in other positions the disease is locally malignant, soon involving the neighboring lymph glands, but seldom setting up

FIG. 81.—Early epithelioma of the lip. (Ewing.)

metastases in the internal organs. The lymphatics from the upper lip to the lateral part of the lower lip drain into the submaxillary glands, those from the central part of the lower lip into the submental glands. From both of these glands infection may pass to the deep superior cervical glands. Even when the floor of the mouth is extensively invaded by the growth it is very seldom that the salivary glands are the seat of metastases. Glandular involvement may be noted within three months, but quite frequently it is delayed for nine or twelve months. It is well to bear two points in mind: (1) the glands may be involved, but may show no enlargement; (2) the enlargement may be inflammatory and not malignant in nature.

Chancre.—Extragenital infection of the lip, usually the upper one, may occur in three ways. (1) A person with active syphilis of the mouth may infect another by kissing. (2) An infant may be suckled

by a syphilitic wet nurse. (3) The spirochete may be conveyed through the use of infected utensils.

The lesion begins as an indurated nodule, which may ulcerate and present the usual appearances of a hard sore. The submental and submaxillary glands on both sides soon become enlarged and hard. Healing takes place at the end of a month or six weeks. In distinguishing the condition from cancer the demonstration of the spirocheta pallida in the discharge from the sore, and the rapid response to antisyphilitic treatment, are of great value.

Other rarer conditions found in the lip are angioma and lymphangioma. An *angioma* forms a localized swelling the surface of which presents a tell-tale bluish tinge. A *lymphangioma* gives rise to a more diffuse enlargement of the lip, to which the term macrocheilia is applied. Both of these conditions are congenital, and usually occur in children.

THE MOUTH

Stomatitis.—Inflammation of the buccal mucous membrane may be catarrhal, ulcerative, or gangrenous.

The *catarrhal* form is common in poorly-nourished children. There is general redness and swelling of the mucosa, or there may be localized grey patches with a sharply defined margin which are often very tender. In the *ulcerative* variety there may be small superficial ulcers, occurring especially at the angles of the mouth, or the destruction may be more general and deep. The *gangrenous* form, also called cancrum oris or noma, starts as a black spot, which soon spreads so as to involve a large area, and is accompanied by severe constitutional disturbance.

The different varieties of stomatitis are all dependent on conditions of lowered vitality, so that treatment must be general as well as local.

Ulcer of the Palate.—The usual cause of ulceration of the palate is tertiary syphilis. Much more rarely it may be due to cancer or tuberculosis.

The *syphilitic* ulcer commences as a gumma. Necrosis occurs, with the separation of a slough, and the ulcer finally perforates the palate, leaving a punched-out opening of varying size through which food regurgitates into the nose.

Rare Conditions.—Tuberculosis and epithelioma may likewise give rise to ulceration and subsequent perforation of the palate, but they are seldom encountered.

THE TONSILS

The tonsils may be red and inflamed as the result of tonsillitis, Vincent's angina, diphtheria, scarlet fever, and syphilis.

Acute Tonsillitis.—Two forms may be distinguished, the follicular and the parenchymatous.

In the *follicular* variety the tonsils are swollen and red, and the surface is dotted with yellowish-white flecks, which are plugs of leu-

cocytes and desquamated epithelial cells projecting from the mouths of the crypts. They can usually be readily wiped off, thus differing from the condition in diphtheria. The inflammation is confined to the lymphoid follicles surrounding the crypts of the gland.

In the *parenchymatous* form or quinsy the inflammation is more general, involving the substance of the tonsil and spreading to the surrounding tissues. The constitutional symptoms are much more severe, and the condition usually goes on to suppuration. The inflammation is often more marked on one side, the uvula is deviated to the opposite side, and the presence of pus is indicated by great swelling of the peritonsillar tissue of the anterior pillars of the fauces. The lymphatic glands of the neck are enlarged and tender.

Diphtheria.—On the inflamed tonsil there is a single grey patch, as contrasted with the multiple patches of tonsillitis. It is rather firmly adherent, and when removed leaves a red raw surface. A similar patch on the soft palate is pathognomonic. The presence of albuminuria and the absence of knee jerks may help in diagnosis. A bacteriological examination for the Klebs-Löffler bacillus must always be made, but in a suspicious case the administration of antitoxin should never be withheld until the report of such an examination is received.

Vincent's Angina.—In this condition a grey membrane is present on the tonsil which may readily be mistaken for diphtheria. Somewhat characteristic is the undue amount of destruction, quite a large cavity being often seen when the slough is removed. The secretion contains two kinds of organisms, a long fusiform bacillus with pointed ends, and a delicate spirochete which stains very faintly with the ordinary aniline dyes. When a swab is taken for diagnostic purposes it should be smeared at once on a glass slide, for the diagnosis is made by smear and not by culture, seeing that the organisms do not grow on the ordinary media.

Scarlet Fever.—The tonsil is red and swollen, and may occasionally present yellow muco-purulent patches. The bright diffuse red color of the throat and soft palate, the strawberry tongue, and the skin rash are points of diagnostic importance.

Syphilis.—Early in the *secondary* stage of syphilis the mouth presents characteristic lesions, which are characteristically bilateral. The tonsils are red and inflamed, and on the surface there are irregular greyish-white patches often likened to snail-tracks. Superficial ulcers may be present. These lesions are not confined to the tonsils, but occur on the fauces, soft palate, and other parts of the buccal mucous membrane.

In the *tertiary* stage deep, punched-out ulcers may be present on the tonsils, fauces, or palate, the result of the breaking down of a gumma.

A *primary* chancre may occasionally be met with on the fauces or tonsils. It is apt to be mistaken for an epithelioma.

Swellings at the Back of the Mouth

A swelling at the back of the mouth may be due to malignant disease, syphilis, retro-pharyngeal abscess, and Ludwig's angina.

Malignant Disease.—*Epithelioma* may commence in the pharyngeal wall, the soft palate, or the tonsil. It forms an irregular, hard, nodular growth, which imparts great fetor to the breath from the accompanying ulceration. The glands at the angle of the jaw are enlarged.

Lymphosarcoma commences in the tonsil, but rapidly involves the surrounding parts, producing great destruction.

Syphilis.—A primary chancre may occasionally develop on the fauces or tonsils. It forms a hard, red mass which may be mistaken for epithelioma. The very early enlargement of the submaxillary glands is of value in differentiation.

Retro-pharyngeal Abscess.—This is a condition in which pus is formed in the loose tissue between the posterior wall of the pharynx and the vertebral column. It may be acute or chronic. The *acute* form occurs in children at the end of a debilitating illness. In addition to marked constitutional symptoms, there is rigidity of the neck, great pain on swallowing, loss of voice, and a tense swelling can be felt—seldom seen on account of inability to open the mouth—on the posterior wall of the pharynx. Prompt incision is indicated.

The *chronic* from is usually the result of tuberculous disease of the cervical vertebræ.

Ludwig's Angina.—This fortunately rare condition is a diffuse streptococcal cellulitis involving the structures at the back of the throat, the tongue, and the neck. The inflammation is intense, and usually proves fatal in a few days.

THE TONGUE

The principal pathological conditions met with in the tongue are acute swelling, chronic glossitis, thickening, and ulcers.

Acute Swelling.—This occurs in *acute glossitis*. It is not a common condition, and may follow the sting of an insect or result from a septic wound. The tongue rapidly becomes very swollen and inflamed, and suppuration may develop, necessitating free incision. Acute swelling may occur apart from inflammation of the tongue. In a case of general urticaria in a young married woman I have seen it in so severe a form that it nearly cost the life of the patient through suffocation.

Chronic Glossitis.—The great cause of chronic thickening of the tongue is tertiary syphilis, and induration of the base of the tongue is recognized as valuable post-mortem evidence of that disease. The condition may occur in two forms, a superficial and a deep.

In the *superficial* form, commonly known as leukoplakia, there is in addition some exciting cause, of which the irritation of a hot pipe

and drinking strong spirits are the two most important. The initial lesion is the typical syphilitic proliferation of connective tissue cells in the deeper layers of the mucosa. This is followed, especially when one of the above-mentioned irritants have been in operation, by a proliferation and heaping up of the cornified epithelium, with the formation of lozenge-shaped, milk-white patches which are crowded together so as to give a mozaic-like appearance to the dorsum of the tongue in its anterior half. Cracks and fissures may appear which are not only very painful and tender, but may form the starting point of an epithelioma.

In some cases proliferation of the epithelium does not occur, and the affected areas present a typical smooth, red, glazed appearance. The smoothness is due to the obliteration of the papillæ by the inflammatory process. A smooth, red and atrophied tongue is very suggestive of syphilis.

In the *deep* form of chronic glossitis there is proliferation of small round cells and fibroblasts, with the formation of a cellular fibrous tissue, which later becomes dense and contracts, giving rise to deep scars, distortion, and atrophy. The tongue is therefore swollen in the earlier, contracted in the later stages. The surface is covered by irregular nodules separated by deep fissures, an appearance highly characteristic of syphilis. Here again malignant disease is a not uncommon complication.

Ulcers.—Ulcer of the tongue may be due to one of those four pathological conditions which confront us at every turn in surgical pathology; inflammation, syphilis, tuberculosis, and malignant disease. Simple (inflammatory) and malignant ulcers are common, syphilitic less so, while those due to tuberculosis are rare. The diagnosis between a syphilitic and a malignant ulcer is often very difficult. If a chronic ulcer in a man of middle age does not respond readily to antisyphilitic treatment, a small piece should be removed for microscopic examination.

A *simple* ulcer usually occurs at the edge or tip of the tongue, and is the result of some source of irritation within the mouth, such as a jagged tooth or an ill-fitting plate. In the early stage it is shallow and inflamed, but if the irritant is not removed the ulcer becomes chronic in character, with indurated edges and a base often covered with a slough. Such an ulcer needs watching, as it may become malignant.

Simple ulcers may also develop on the dorsum of the tongue in the deep fissures of chronic glossitis, but these ulcers must always be looked upon with the greatest suspicion.

A *malignant* ulcer is produced by the ulceration of an epithelioma. The disease is much commoner in men, about 85 per cent, of the cases occurring in the male sex. The usual age period is between 40 and 60, but it may occur earlier or later.

It is probable that cancer rarely, if ever, develops in a perfectly healthy tissue, and this truth has its most brillant illustration in the case of cancer of the tongue. Such conditions as chronic ulcers from

local irritation, patches of leukoplakia, and the deep fissures of chronic glossitis are the only too common precursors of malignant disease, and the high incidence in man is due to the fact that these precancerous conditions are much commoner than in women.

The condition begins as an excoriation, a crack, or a flat nodule which soon becomes ulcerated. The common position is at the edge of the tongue in its anterior two-thirds, that part being more liable to irritation. In those cases in which malignant disease develops on top of a chronic glossitis the dorsum may be affected. It may extend superficially, giving rise to a warty, ulcerated, fungating mass, or deeply, in which case the ulcer is not raised.

The nearest lymphatic glands, the submaxillary and the sublingual, may become enlarged at an early stage, and the cervical lymphatic glands may be involved about the same time. The salivary glands are usually removed by the surgeon, but Dudgeon and Mitchiner have shown in a recent communication that, although these glands are frequently the seat of chronic inflammatory changes somewhat analogous to the changes met with in the pancreas in chronic pancreatitis and apparently due to infection passing along the ducts from the mouth, yet they very rarely show carcinomatous deposits. These investigators found that the lymph glands showed malignant changes in only 27 per cent of early and 50 per cent of late cases, although inflammation was always present.

The chief characteristic of the malignant ulcer is the dense, almost cartilaginous, hardness of the floor and edges. The latter are often raised, but they may be level with the rest of the tongue. Difficulty may be experienced in distinguishing it from an ulcerating gumma and even a chronic simple ulcer. When in doubt remove a piece for microscopic examination.

Syphilitic Ulcer.—A primary *chancre* may occur on the tongue. It presents the usual appearance of a hard sore, and the spirochæta pallida is present in the discharge. The glands in the floor of the mouth are enlarged.

In *secondary* syphilis the mucous patches frequently present on the dorsum of the tongue may become ulcerated. The tortuous outline of the edge is somewhat characteristic. Numerous spirochetes are present in the discharge. The lesion heals under treatment leaving a silvery stellate scar.

In *tertiary* syphilis ulceration occurs as the result of the breaking down of a gumma, or more rarely it may following syphilitic glossitis. It may be very difficult to distinguish this variety of ulcer from epithelioma. The ulcer is more likely to be syphilitic if it occurs on the dorsum, if the induration is not very marked, and if the neighboring glands are not enlarged.

Tuberculous Ulcer.—It is said that tuberculosis of the tongue may occur as a primary condition, but for practical purposes it is always secondary to tuberculous disease of the lung. In any case it is a rare disease. The ulcer presents the oval outline, sinuous edges, pale

watery-looking granulations, and absence of induration characteristic of tuberculous lesions elsewhere. In rare cases the disease begins as a nodule instead of an ulcer, but ulceration develops later.

Tuberculosis chooses the tip, as epithelioma the edge, and syphilis the center of the tongue, but of course any of these conditions may occur in any part of the organ.

Ulcer of the Tongue

Variety	Site	Character	Remarks
Inflammatory	Edge or tip.	Shallow and inflamed.	Assoc. with sharp tooth or plate.
Malignant	Edge or center.	Hard. Begins as crack or nodule.	May be assoc. with chronic glossitis. Lymph glands enlarged.
Syphilitic	Dorsum.	Serpiginous in outline.	May be primary, secondary, or tertiary.
Tuberculous	Tip.	Undermined edge. No induration.	Always secondary.

Rare Conditions.—Sarcoma and various forms of innocent tumors may occur in the tongue. Of these the commonest is the angioma, which appears as a soft rounded mass, with a blue or purple tinge. The condition is congenital.

Dermoid cysts may occur beneath the tongue. They may project under the chin or into the floor of the mouth. A thyroglossal cyst or tumor may arise in the tongue at the upper end of the thyroglossal duct. This condition is considered on page 225.

Macroglossia, as the name implies, is not a pathological entity. The term is generally applied to a diffuse congenital enlargement of the tongue due to lymphangioma. Marked enlargement is found in cretinism, and is occasionally present in acromegaly.

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CHAPTER XVI

THE STOMACH AND DUODENUM

The stomach and the duodenum as far as the entrance of the common bile duct have a common development and blood supply, possess acid contents, and are subject to similar diseases. They will therefore be considered together. Both are developed from the fore-gut, and are supplied with blood by the celiac axis. The remaining part of the duodenum is derived from the mid-gut, and is supplied by the superior mesenteric artery.

Two diseases of the stomach overshadow all others in frequency and importance. These are ulcer and cancer. They will therefore be considered first.

GASTRIC ULCER

Gastric ulcer may be acute or chronic. This, though a simple statement, is of such far-reaching application to such questions as the relation of sex and age to the ulcer, the site of the ulcer, etc., that it must never be lost sight of.

Every ulcer commences as an acute ulcer. In very many cases this gives rise to no clinical symptoms, the ulcer heals in the course of three or four weeks, and leaves a scar which it may be impossible to detect without the most searching examination.

Bolton in his monograph on the subject insists that gastric ulcer is no mysterious entity, no disease process due to one special and peculiar cause. Just as ulcers may occur in various parts of the body —skin, gums, etc.—from a variety of local or general causes, so may they occur in the stomach. The presence of the gastric juice, however, provides a factor which greatly facilitates the ulceration process once it is started. Why some ulcers should heal readily and others should refuse to do so and become chronic we do not really know, but exactly the same phenomenon is encountered in ulcers of the skin.

Sex and Age.—It used to be considered that gastric ulcer was essentially a disease of young women, a conclusion based upon clinical evidence. A study of the "pathology of the living" on the operating table has shown that when the stomach of many of such patients is opened no trace of ulcer can be found. In some of these cases a condition of septic gastritis has been present. In others the stomach has appeared quite normal. Moreover the stomach is by no means the only organ which manifests disturbance by the appearance of gastric symptoms. The gall-bladder and the appendix may be cited as main offenders in this connection, but other parts of the alimentary canal

may also be at fault. As Moynihan says, the stomach is so sensitive an organ that it cannot refrain from weeping when its neighbors are in trouble, and its voice is sometimes so loud as to drown that of the real sufferer.

For these reasons it has been necessary to alter our views on the relation of age and sex to gastric ulcer. In the post-mortem room an open ulcer is found with about equal frequency in men and women; in young women the acute type is common, but the chronic type is more frequent in men between forty and fifty. Operating room results show that whilst an acute perforating type of ulcer is more common in women under the age of twenty-five, the usual chronic ulcer of medical practice is seen in men of middle age.

Etiology.—It has already been remarked that just as ulcers elsewhere may be produced by various agencies such as trauma, interference with the blood supply, bacterial infection, etc., so in the stomach there is no one and only cause. A gastric ulcer arises from the same type of lesion as precedes ulcer in other parts of the body, but it owes its peculiar appearance, in which it differs from all other ulcers, to the action of the gastric juice. Moreover a comparatively trivial lesion, which in the skin would never develop into a sore, will rapidly become converted into an ulcer in the stomach owing to this same digestive action.

The two common lesions which may precede the development of an acute ulcer are (1) local necrosis of the mucous membrane; and (2) local hemorrhage into the mucous membrane.

1. *Local Necrosis.*—Although there is an extremely large variety of ways in which necrosis may be induced experimentally, it is probable that the methods of production in the human stomach are much more limited.

Of these *bacterial infection* is the most important. In many acute infectious fevers one or more acute ulcers may develop in the stomach. Similar ulcers have been found in experimentally produced septicemia. In many cases minute plugs of bacteria may be demonstrated in the vessel supplying the ulcer. That the process is not merely embolic in nature is shown by the fact that injections of diphtheria toxin by Rosenau and Anderson produced a similar result.

An acute ulcer may arise from a distant local septic focus as well as from a general septicemia, and it is more than likely that in the future this mode of infection will come to be regarded as of extreme importance. The experimental work of E. C. Rosenow has shown that certain strains of streptococci of low virulence possess an elective affinity for particular tissues such as the stomach, and that these organisms when present in a focus of infection in a tooth abscess, the tonsil, the appendix, or the gall-bladder, may be carried by the blood or lymph stream to the stomach and there set up an acute ulcer.

Local necrosis of the mucosa of both stomach and duodenum may follow *burns of the skin*, with the production of acute gastric or duodenal

ulcer. This is most probably due to the action of a poison of metabolic origin but of unknown nature.

That such a poison may indeed produce areas of local necrosis in the stomach of animals has been beautifully shown by Bolton. An emulsion of the gastric mucous membrane of the guinea pig is injected intraperitoneally into a rabbit at weekly intervals until an efficient "*gastrotoxic serum*" is produced, which, when mixed with the gastric mucosa of a guinea pig in a test tube, will produce destruction of the cells. When this serum is injected into a live guinea pig it will cause local necrosis in the stomach with the formation of one or more acute ulcers.

Necrosis may be caused by unsuitable substances taken *by mouth*. Corrosive poisons offer, of course, an obvious example, but irritants such as alcohol may excite a gastritis which may pass on to local necrosis. The necrosed patch is then digested by the gastric juice, and an ulcer results.

Other conditions such as venous congestion, the pressure of a tumor, etc., may give rise to necrosis in some cases.

2. *Local Hemorrhage.*—Hemorrhage is often combined with necrosis, and may be secondary to that process. In many cases, however, it occurs alone or as the primary event. The commonest cause is bacterial infection, either owing to the effect of the bacteria on the vessel wall or to embolic plugging of a small vessel.

The vitality of the mucous membrane into which the hemorrhage has occurred is so lowered that necrosis and ulceration are the natural consequence.

Acute Ulcer.—More often than not the ulcers may be multiple, and as many as six may be present at once.

The ulcer is *situated* on the anterior or posterior wall near the lesser curvature, and is more often found in the cardiac than in the pyloric half of the stomach, thus differing from the chronic ulcer. This simply means, of course, that ulcers in the cardiac half heal with greater readiness than those in the pyloric half.

The *size* varies considerably. Sometimes it is no larger than a pin's head, or it may appear in the unstretched stomach as a slit-like fissure. Others are larger, but seldom exceed an inch in diameter. A small acute ulcer is easily overlooked at autopsy, even though it be the cause of fatal hemorrhage, for the absence of any thickening of the mucous membrane makes the ulcer appear very shallow.

The *appearance* is that of a cleanly punched-out hole, the bottom of which is of a deep red color. The edge is sharply cut, owing to the digestive action of the gastric juice. It is this characteristic which distinguishes it from a simple ulcer in any other part of the body. The surrounding mucous membrane is often quite healthy, or it may show some edema or a few scattered hemorrhagic spots.

The peritoneum may be *perforated*, the opening being usually smaller than the ulcer, but sometimes the appearance is such as to suggest that a hole had been punched right through the stomach wall.

In any case the funnel-shaped appearance so characteristic of chronic ulcer is never seen.

A blood vessel may be opened into, even by a very small ulcer, and fatal *hemorrhage* may result. In the fatal cases an artery is the vessel involved.

Microscopically there is always evidence of inflammatory reaction, although in some cases the reaction appears to be very slight. The mucous membrane at the edge shows capillary congestion and infiltration with inflammatory cells. The glands in the vicinity are distinctly degenerated. The submucous coat shows no thickening, a point of great importance.

Symptoms.—An acute ulcer usually gives rise to no symptoms, unless it announces its presence by the catastrophies of hemorrhage or perforation. When either of these occurs in a young woman who has hitherto been in apparently perfect health, it is probably a case of acute gastric ulcer. In exceptional cases the ulcers may cause pain and vomiting, but these are in no way characteristic, and are more frequently found in patients who have no acute ulcer.

Three things may happen to an acute ulcer; (1) It may heal; (2) it may spread; or (3) it may remain stationary and become a chronic ulcer.

In the majority of cases *healing* occurs readily and completely. By the end of the third week the ulcer is replaced by a scar which is covered by a newly-formed rudimentary mucous membrane. Such scars are very easily overlooked, and have therefore to be searched for with great care.

A *spreading* ulcer may present two very different appearances, depending upon whether the extension occurs laterally or deep. In the former case the ulcer is spread over a comparatively wide surface, but is shallow in depth. In the latter the mouth is not wide, but the ulcer is deep and funnel-shaped.

Chronic Ulcer.—A chronic ulcer is usually single, but several may be present.

The common *site* is the lesser curvature and the posterior surface near to the pyloric end. Over 75 per cent of chronic ulcers occur in this region.

The *size* varies, but the diameter is rarely less than half an inch, and usually from one to two inches.

The *shape*, as in the spreading ulcer, may be funnel-like and deep, or more extensive and shallow. The former is the more common. The walls of the cavity slope steeply downwards like the sides of a cone, or they may descend by a series of steps, giving a terrace-like effect.

The *edges* are thick, raised, indurated, and in many cases overhanging, sometimes to a very marked degree.

The *peritoneal* surface presents a white patch corresponding to the floor of the ulcer. There may be considerable thickening owing to the chronic inflammatory process. Puckering of the surface may be noticeable.

Microscopically the chief difference in the chronic from the acute ulcer is the remarkable thickening of the submucous coat. This

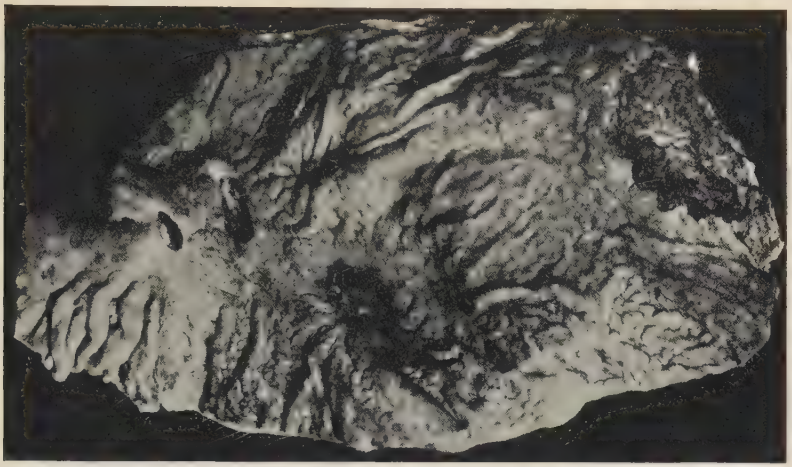

Fig. 82.—Multiple ulcers of the stomach.

Fig. 83.—Ulcer of stomach, showing extreme fibrosis of the submucosa.

thickening consists of a fine connective tissue containing many cells and blood vessels. It is shaped like a wedge, the base of which rests

on the edge of the ulcer. The mucous membrane is infiltrated with round cells, and there is a varying degree of gastritis in the neighborhood.

As digestion is continually proceeding at the base of a chronic ulcer it follows that *perforation* will occur sooner or later. The disastrous consequences of such an event are often minimized owing to adhesions having formed between the floor of the ulcer and some solid organ, of which the pancreas is the commonest, the liver the next in frequency. After perforation a new base for the ulcer may thus be provided by the pancreas or the liver. The pancreas is fairly resistant to the action of the gastric juice, but an interstitial inflammation is set up which converts the surface into a hard sclerotic mass. In the liver

FIG. 84.—Perforated gastric ulcer.

necrosis may be combined with inflammation, so that an abscess cavity may be formed, with subsequent infection of the peritoneal cavity.

Hemorrhage may occur, as with the acute ulcer. If a small artery or vein be opened the hemorrhage will be slight, blood darkened to acid hematin by the hydrochloric acid may be vomited or passed by the bowel, or the amount may be so small that chemical tests for "occult blood" in the feces may be necessary.

If a large artery be opened there will be profuse vomiting of blood, which may prove fatal. Death may occur before any blood is vomited, in which case the stomach will be occupied by a large blood clot.

Symptoms.—Whilst the presence of an acute ulcer may first be announced by the occurrence of such an accident as hemorrhage or perforation, a chronic ulcer is accompanied by symptoms over a period of months or years. Nevertheless a chronic ulcer is a really difficult condition to diagnose, and it may be so readily simulated by other

conditions that for scientific data only those cases which have been demonstrated on the operating table should be accepted as chronic ulcers.

Pain is the most characteristic symptom. It usually bears a definite relation to food, being relieved by the taking of food, and coming on from one to two hours after the meal. As Moynihan says: "The constancy of the sequence—food, comfort, pain; food, comfort, pain—is the most important of all the clinical matters concerned with the diagnosis of gastric ulcer."

The pain is not due, as used to be thought, to the action of the gastric juice on the ulcer, but to what Cannon has called the "hunger contractions" of the stomach, which are stilled by the administration of food. There are curious and inexplicable intermissions in the attacks of pain, lasting sometimes for months. Even during these intermissions, however, there is always a sense of gastric discomfort.

There are other symptoms, of which vomiting is the chief, but it would be out of place to discuss them here.

Cicatricial Contraction.—In course of time a chronic ulcer may heal partially or wholly, although the greater the thickening of the submucous coat, the less likely is this to occur. In the process of healing, and even in ulcers which have failed to heal, there may be great cicatricial contraction. If this occurs at the pylorus it will produce *pyloric stenosis* with dilatation of the stomach. If it occurs on the lesser curvature it will produce *hour-glass contraction*, by which the stomach is divided into two compartments, owing to the greater curvature being drawn up towards the lesser.

DUODENAL ULCER

An ulcer similar in all respects to gastric ulcer occurs in the supra-ampullary part of the duodenum, for this part of the duodenum contains acid gastric juice.

The *acute* ulcer may occur at any age, and is often a complication of an acute fever. A relationship certainly exists between chronic appendicitis and gastric or duodenal ulcer. Acute ulcers complicating burns are commoner in the duodenum than in the stomach.

The *chronic* ulcer is much commoner among men than women, more than 70 per cent being in the male sex. The usual age is between 30 and 50. Over 95 per cent of the ulcers are found within an inch of the pylorus, usually on the upper or anterior wall. Wilkie has pointed out that the portion of the duodenum usually affected by ulcer is supplied by the supraduodenal artery, which is practically an end artery. It is more than possible, therefore, that vascular occlusion may play an important part in the production of duodenal ulcers.

Frequency.—Ulcer of the duodenum used to be regarded as a rarity in comparison with ulcer of the stomach. Observations on the operating table have shown that it is a remarkably common condition. It is still difficult to give with exactness the relative frequency of gastric and duodenal ulcer. W. J. Mayo considers that in

60 per cent of cases of peptic ulcer the ulcer is situated in the duodenum, and the experience of many surgeons such as Moynihan who see large numbers of cases is similar. It must be borne in mind, however, that the surgeon sees a special group of cases, those, namely, in which obstructive symptoms are a prominent feature. If all ulcers are taken into consideration it is probable that the greater number will be found in the stomach. Einhorn gives the following table in the Nelson Loose-Leaf Medicine.

Localization of Peptic Ulcer

	Cardia	Lesser curvature	Pylorus	Duodenum
Males	6	40	17	37
Females	14	47	17	22

The *symptoms* are similar to those of gastric ulcer, but the two conditions can usually be readily distinguished from one another. Pain does not come on until two hours after a meal, and continues until the next meal is taken, when it is at once relieved. The peculiar

Fig. 85.—Perforated duodenal ulcer. The pyloric end of the stomach has been laid open.

remissions of pain already referred to are much more complete in duodenal ulcer than in ulcer of the stomach.

Perforation is a more common complication than in gastric ulcer, for ulcer of the duodenum chiefly affects the anterior wall, ulcer of the stomach the posterior wall.

Secondary Jejunal Ulcer.—It not infrequently happens that after the performance of a gastro-enterostomy a secondary ulcer develops either at the gastro-jejunal junction or in the jejunum itself within a few inches of the opening and nearly always in the efferent loop. The former is called a gastro-jejunal, the latter a jejunal ulcer. It is impossible to estimate with any accuracy the frequency of the

condition. Paterson suggest 1.5 per cent, but this appears an unduly high figure. The ulcer develops much more frequently after anterior than posterior gastro-enterostomy.

The lesion may be an acute perforating ulcer or a chronic ulcer, and in each case resembles the corresponding condition in the stomach or duodenum. Wright, in a careful study of the subject, points out that the course of the chronic ulcer depends on the nature of the gastro-enterostomy. If this has been of the anterior type the ulcer tends to adhere to the anterior abdominal wall, and a large tumor is produced in this situation. In the ulcer following the posterior type of operation the inflammatory mass is not so evident, because it is hidden behind the colon and mesocolon. If healing occurs the resulting fibrosis may lead to a severe degree of stenosis. This is most marked in the gastro-jejunal type of ulcer, where it may be so extreme as to lead to stenosis of the opening.

The exact *etiology* of the condition is still a matter of debate. The essential cause is doubtless the action of the acid gastric juice upon the mucosa of the jejunum which is not intended to resist such action. It is well known that the complication practically never occurs in malignant cases where the gastric acidity is very low, and is commonest in cases of gastric ulcer, where it is often exceptionally high. The experimental work of Wilkie has shown that the action of the gastric juice alone is not sufficient to produce an ulcer in the mucosa of the healthy jejunum. Some other factor must be present. In most cases, especially of gastro-jejunal ulcer, there is local injury of the mucosa produced by the presence of a continuous unabsorbable suture. In some cases the predisposing cause originally responsible for the gastric or duodenal ulcer may weaken the jejunal mucosa, and thus allow the eroding action of the gastric juice full play.

CARCINOMA

Cancer of the stomach is one of the terrible diseases. About 30,000 deaths from cancer of the stomach occur in the United States each year. It is commoner in men than women in the proportion of about 60 to 40. The stomach is the most common seat of cancer in men, as the uterus is in women. The usual age is between 40 and 60.

The disease appears to be unduly prevalent in certain families. The most famous example is that of Napoleon I, who died of cancer of the stomach, as also did his father, his brother, and two of his sisters.

Site.—Of all gastric cancers 60 per cent begin in the pyloric region, 20 per cent along the lesser curvature and cardia, and most of the remaining 20 per cent along the greater curvature. Very few commence in the fundus.

Relation of Gastric Ulcer to Carcinoma.—It was Rokitansky who in 1840 was the first to recognize that cancer may develop upon a gastric ulcer. Since that day, and particularly within recent years, much attention has been devoted to the subject, and the most widely divergent views are held regarding it.

Moynihan, in a recent Hunterian Lecture, considers that two out of every three cases of gastric carcinoma which he sees on the operating table give a past history very suggestive of ulcer, and he states that in 18.5 per cent of excised chronic ulcers which have no gross appearance of malignancy microscopic evidence of early carcinoma may be found in the edge of the ulcer. Sherren, on the other hand, in a series of similar cases found malignant change in only 4.4 per cent, and Paterson finds that only 1 per cent of his cases of gastric ulcer diagnosed by operation subsequently develop cancer. The most remarkable and the most frequently quoted statistics are those from the Mayo Clinic. Wilson and MacCarty, from an investigation of a large mass of material, came to the conclusion that 71 per cent of cases of cancer of the stomach originate in simple ulcer, and in a later communication MacCarty states that 68 per cent of apparently simple ulcers show microscopic

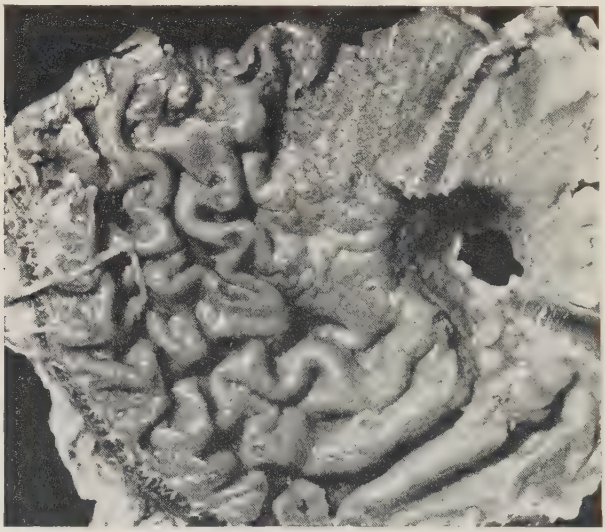

Fig. 86.—Ulcer of stomach with carcinomatous change.

evidence of cancer. He considers that most chronic gastric ulcers larger than 2 cm. in diameter are carcinomatous.

The explanation of these extremely different results is to be found in the attitude of the microscopist who examines the sections. To one man the presence of isolated epithelial cells and atypical tubules in the neighborhood of an ulcer spells carcinoma, whilst to another they are merely a part of the regenerative process. The latter view is well expressed by Spilsbury in the following words: "There are commonly found at the edge of the ulcer gland cells which have penetrated deeply into the scar tissue and are cut off from the regenerating glands. They may exhibit an atypical glandular arrangement, or may form narrow columns of cells; isolated cells are also seen. It is these cells detached from the regenerating epithelium and buried in the fibrous

tissue of the ulcer which are sometimes referred to as precancerous, and which, from their position and irregular arrangement, are regarded by others as indicating malignant transformation in the ulcer."

It seems hardly possible to hope for unanimity in pathological opinion on this matter, for there is no objective method by which we can decide whether or not a cell is malignant, and the large subjective factor must inevitably lead to widely differing results. There can be little room for doubt that a carcinoma *may* develop on top of a chronic ulcer. It would be surprising if this did not occur when we consider the relation of cancer to ulcer in other parts of the body, as for instance in the tongue. The difficulty is to determine the relative frequency

FIG. 87.—Hauser's figure of peptic ulcer with secondary carcinoma of stomach. Note isolated polypoid outgrowths on edge of ulcer and elsewhere. (Ewing.)

with which this does occur. The influence of the answer to this question on the prognosis and treatment of chronic gastric ulcer is evident; if 68 per cent of the apparently simple gastric ulcers seen by the surgeon are in reality carcinomatous, then there is little place for the medical treatment of the condition.

In view of the above considerations it may well be that this essentially pathological question will have to be settled by clinical investigation. A very careful study along these lines, checked by thorough microscopic examination has been made recently by John Morley. He finds the irregularity of the glandular epithelium at the edge of the chronic ulcer already referred to, and even an apparent invasion by

some tubules below the line of the muscularis mucosæ, but he adds "the grouping of tubules in their suspicious surroundings is so similar in arrangement and so circumscribed in extent that I have formed the opinion quite definitely that it is merely an infolding of the epithelial edge by scar tissue in an attempt at healing, and is not evidence of a malignant change."

In his clinical investigation Morley finds that the average duration of pre-operative gastric symptoms in histories taken either by himself or carefully supervised by him was 12.7 months in the case of cancer and 10.3 years in the case of ulcer. The average age of onset in ulcer was 32.8 years, whereas in cancer it was 49.9 years. A somewhat similar investigation of a series of 221 ulcer patients was recently conducted by Nielson (quoted in Morley's paper), who followed some of the cases for a period of 19 years. He also comes to the conclusion that the transformation of a simple ulcer into a malignant one is not a common occurrence. Ulcer of the duodenum, it may be

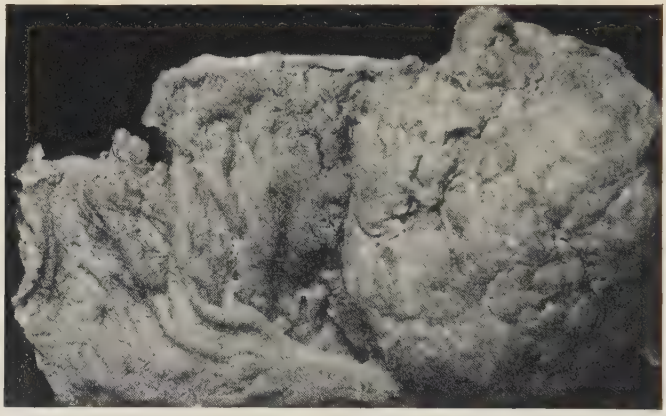

Fig. 88.—Polypoid form of carcinoma of stomach.

recalled, is very common whilst cancer of the duodenum is extremely rare.

Superficial cancers of the stomach often become ulcerated quite early, and these must not be mistaken for a chronic ulcer showing secondary malignant change. Such ulcers are comparatively superficial, whereas the true peptic ulcer becoming malignant is deep and crater-like with a very thick base. In an ulcer which has been carcinomatous from the beginning the base as well as the edges show the structure of carcinoma, whereas in the ulcer which becomes malignant the change is found in the edge but not in the base, for the latter is densely fibrous and resists invasion. The malignant change is usually found on the pyloric edge of the ulcer.

The classification of the various forms of gastric carcinoma is by no means easy. The chief type of growth is the adenocarcinoma, but

in those forms in which there is much infiltration of the stomach wall, especially when combined with an abundance of the stroma, the glandular arrangement may be completely lost, and the appearance may be that of a carcinoma simplex, especially the scirrhous variety.

In our classification, therefore, we shall rather be guided by the gross form than by the microscopic appearance. The various tumors may then be divided into: (1) a polypoid form, (2) a sessile form associated with ulceration, (3) an infiltrating form in which there is no ulceration, (4) colloid cancer.

1. **The Polypoid Form.**—This variety may commence in any part of the stomach. A large, soft, fungating mass, friable and easily

FIG. 89.—Fungating carcinoma of the stomach.

disintegrated, projects into the lumen, and may fill up the greater part of the cavity. The surface is ulcerated and sloughing, bleeds at a touch, and the whole looks terribly malignant. Nevertheless the outlook is probably better in these cases than in those about to be described, for metastases do not occur so readily, the lymph nodes are not involved so early, and the invasion of the stomach wall may not be extensive. There may be a remarkable absence of prominent gastric symptoms, but, as in other parts of the body, ulceration rapidly transforms the clinical picture for the worse, accompanied as it is by hemorrhage, pain, vomiting, and cachexia.

Microscopically the growth is an adenocarcinoma, and consists of atypical tubular spaces lined by proliferating epithelium. Although

the disease commences in the mucosa, it soon breaks through the muscularis mucosæ and appears in the submucous and deep coats.

2. **The sessile form** is the commonest variety. It occurs chiefly at the pylorus and on the lesser curvature. Ulceration takes place early, so that the growth appears as a crater-like ulcer of varying dimensions, with raised, thick, rounded edges. Just beyond the edge although the mucosa appears normal and velvety it will be found impossible to pick it up from the underlying tissues.

This is the form taken by a carcinoma which originates in a gastric ulcer. In such a case the ulcer presents the usual appearance of a peptic ulcer. The base, which is thick and very dense, is free from

Fig. 90.—Adenocarcinoma of stomach. There is a very sudden change from the normal mucosa to the wildly proliferating epithelium. The cells of many of the new glands stain darkly.

cancer, the characteristic changes being found in the edges, particularly the side nearest the pylorus. If carcinomatous changes are found in the base, the condition is probably one of primary carcinoma with secondary ulceration.

The cut surface shows a firm greyish-white tissue, often flecked with yellow necrotic areas, causing thickening of the submucosa, penetration of the muscular coat, and thickening again of the subserous tissue. From the outside the position of the tumor may be recognized by the rigidity of the stomach wall and the possible presence of small

nodules of growth on the peritoneal surface. The lymph glands along both the lesser and greater curvatures may display white metastatic

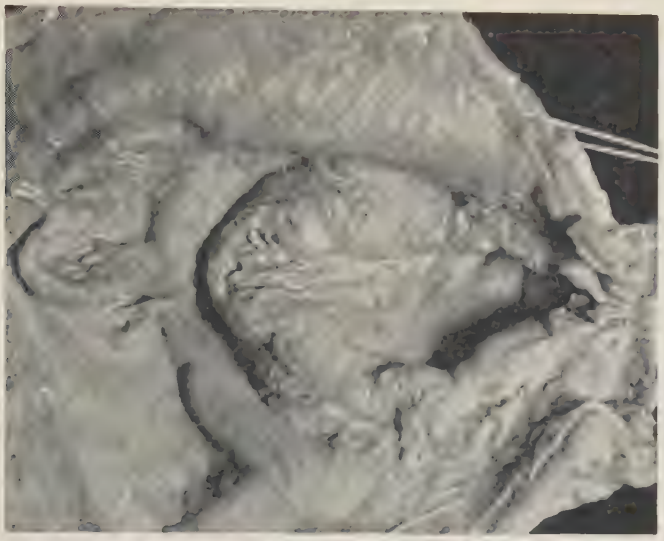

FIG. 91.—Carcinomatous ulcer of stomach.

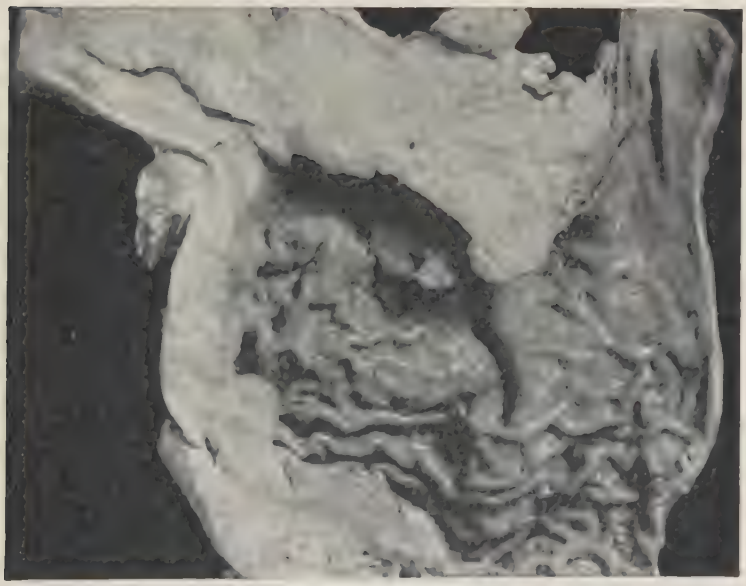

FIG. 92.—Carcinoma of the cardiac end of the stomach invading the esophagus (viewed from behind).

deposits, and the omentum may be studded with similar nodules. The liver is invaded either by direct spread or through the portal vein.

Enormous growths in the liver may be secondary to quite a small nodule in the stomach. The supraclavicular glands on the left side are enlarged in about 3 per cent of cases, owing to spread along the thoracic duct.

Microscopically the growth may be an adenocarcinoma, but in many cases it is a medullary cancer.

3. **The Infiltrating Form.**—Instead of growing into the lumen to form a projecting mass, the tumor cells may infiltrate the wall, either forming a densely hard ring surrounding the pylorus, or giving rise to a general thickening and induration of the stomach wall, with marked shrinkage in size, but little or no ulceration. The mucosa is adherent to the underlying tissues, and the latter condition is that which used to be known as leather-bottle stomach.

Microscopically the condition is one of scirrhous carcinoma, with extremely dense and abundant stroma, the epithelial cells being

FIG. 93.—Leather-bottle stomach, showing small size of stomach with extreme thickening of wall.

scattered here and there in small groups or as single cells. In some areas they may have entirely disappeared.

Linitis Plastica.—This is an obscure condition to which a variety of names have been given, such as cirrhosis of the stomach, fibromatosis of the stomach, leather bottle stomach, etc. Many cases are merely

examples of very diffuse scirrhous carcinoma, but whether all belong to this category it is impossible at present to say.

The cavity of the stomach is much diminished in size, and the walls are enormously thickened, the thickening being most marked in the submucous coat. When the wall is incised it may feel like cartilage. The pylorus projects into the duodenum like the cervix uteri. The outside has a peculiar pearly appearance.

The microscopic picture is one of dense fibrosis. In this fibrous tissue a few small densely staining carcinomatous cells may be found, but often all trace of these has vanished. The cells appear to have a limited growth capacity, so that spontaneous regression of the tumor occurs, although this is not sufficient to save the life of the patient.

4. **Colloid cancer** is merely a degeneration form of one of the other varieties. The tubules become dilated into cyst-like cavities contain-

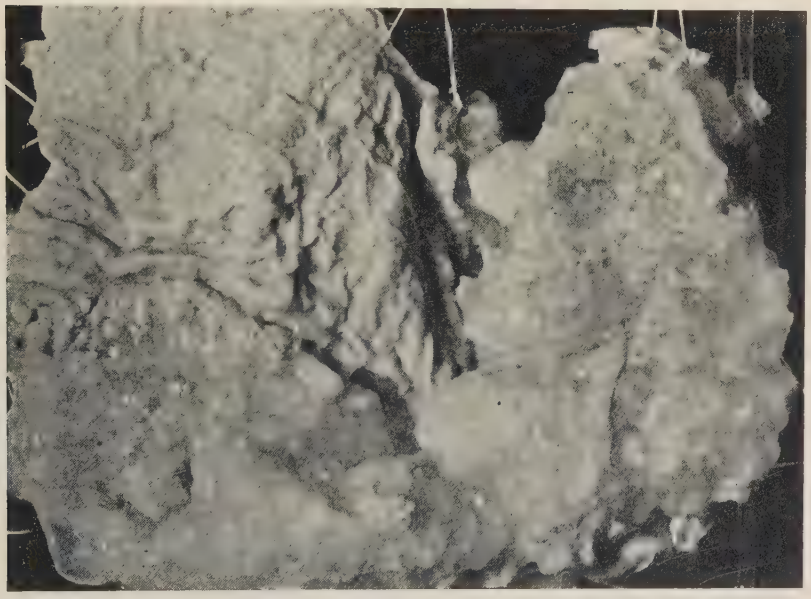

FIG. 94.—Colloid carcinoma of stomach.

ing a gelatinous material. There is great thickening of the stomach wall, and a large ulcerated gelatinous mass having the appearance of sago pudding projects into the cavity. The great omentum may be infiltrated with similar material. The metastases have the same character as the primary growth.

Spread.—The disease may spread: (1) through the stomach itself; (2) to neighboring organs; and (3) to distant parts.

In the *stomach* the carcinoma extends mainly in the submucous coat. It is a remarkable fact that the duodenum is practically never involved. The nearest lymphatic glands are practically always involved by the time the case comes to operation. In the earlier cases

the glands along the lesser or greater curvatures are infected; in the later those at the hilum of the liver, those around the celiac axis, and the superior mesenteric glands. Reference has already been made to enlargement of the supraclavicular glands.

Of the *neighboring organs* those most commonly affected are the liver, the pancreas, and the colon. The liver is involved in about 33 per cent of autopsy cases. Secondary growths in the omentum are

FIG. 95.—Colloid cancer of stomach. The submucosa is invaded by carcinoma cells which have undergone an extreme degree of colloid degeneration.

common, and the ovaries are involved in 2 per cent of the cases. This involvement is frequently bilateral, and is due to implantation spread of the carcinoma cells over the surface of the peritoneum. In some cases the structure is that of the so-called Krukenberg tumor of the ovary, and consists of large cells filled with clear mucoid material which presses the nucleus to one side so as to give a signet-ring appearance.

Secondary growths in the omentum are common, and I have seen several cases at autopsy where the carcinoma cells were carried down over the peritoneum and set up secondary growths in both ovaries.

Metastases may be set up in *distant organs* by the blood stream.

Stomach Contents.—Although an examination of the stomach contents is of comparatively little use in gastric ulcer, it is of the greatest value in arriving at a diagnosis in carcinoma. Several or all of the following may be present.

1. Great diminution or complete absence of free HCl.
2. Low total acidity.
3. Presence of occult blood in the feces as well as in the gastric contents.
4. Presence of lactic acid.
5. Presence of Oppler-Boas bacilli.

Curability.—It is difficult from a study of statistics to say what exactly are the prospects of cure which the surgeon can offer a patient. In a series of selected cases the results may be fairly encouraging. The Mayos report that 20 per cent of their cases were well after three years. Paterson considers that 8 per cent of resections may be surgically cured. In ordinary surgical work the prospect for the patient is very much worse. Much depends on the type of the tumor. The prognosis is very much more favorable in the bulky adenocarcinoma form than in the infiltrating scirrhous variety. In the carcinoma which develops on top of a gastric ulcer there is also a fair chance of recovery. Some of the statistics for this class of case may be criticized on the ground that changes in the ulcer which have been interpreted as carcinomatous in nature may not be really so.

Carcinoma of the Duodenum.—Cancer of the duodenum is remarkably rare in comparison with the similar disease of the stomach. Deaver has collected figures of 151, 201 autopsies, and in only 50 of these was duodenal carcinoma found.

The usual site for the tumor is the second portion of the duodenum, due, probably to the presence of the ampulla of Vater in that part. The ampulla or its immediate neighborhood is a common starting point of the disease. The relative frequency of the various sites is given by Deaver as follows: first part, 22.15 per cent; second part, 65.82 per cent; third part 12.03 per cent.

Carcinoma of the first portion usually arises as a malignant degeneration of a chronic duodenal ulcer. Such an occurrence, however, is very rare compared with the case of ulcer of the stomach. The characters of the growth are similar to those of gastric carcinoma. Usually the tumor is of the flat ulcerating variety. Cancer of the second portion is frequently associated with dilatation of the biliary and pancreatic ducts, with the production of jaundice, and the formation of pancreatic retention cysts. In the only example of the disease which has come under my notice the dilatation both of the bile and the pancreatic ducts was so pronounced as to be one of the

chief features at the autopsy. When the liver was cut the bile ducts could be seen standing out in a remarkable manner, the surface of the pancreas was covered by numerous cysts about the size of a pea, and the main pancreatic duct was greatly dilated.

ACUTE DILATATION OF THE STOMACH

A surgical complication, as mysterious as it is alarming, is acute dilatation of the stomach. It may occur as a sequel to a surgical operation, or as a complication of some other disease. The operation which it complicates is usually an abdominal one, but occasionally it may be on other parts of the body. The onset may be of dramatic suddenness; in some of the recorded cases the stomach has attained an extreme size in less than a minute. The most prominent symptoms are vomiting, epigastric pain, distension of the abdomen, and collapse.

The stomach, when examined post-mortem, is found to be enormously distended, often extending as far as the symphysis pubis. The contents of the stomach in the early stages are entirely gaseous, but later great quantities of fluid may be present. The two most successful methods of treatment, the use of the stomach tube and the prone position, are designed to combat respectively the accumulation of gas and of fluid. The gastric wall is extremely thin, and the mucosa may be fissured and eroded. The dilatation in some cases ends at the pylorus, in others it extends as far as the point at which the duodenum is crossed by the superior mesenteric vessels, whilst in still others it extends beyond that point. The small intestine is collapsed and hangs down into the pelvis.

Etiology.—The exact method of production of acute dilatation of the stomach is still a matter for debate. The popular view used to be that the dilatation was secondary to pressure of the superior mesenteric vessels on the duodenum. While this may be true in some instance, Doolan and others have marshalled such an array of facts against this hypothesis as to make it quite untenable in the majority of cases. To mention but one, such an obstruction can not be demonstrated in more than 25 per cent of cases.

The gastric dilatation, then, must be regarded as a primary and not a secondary phenomenon. Apparently the first step is the production of a paralysis, or rather an atony, of the stomach wall. This is probably reflex in origin, and is occasioned by operative insults particularly to the abdominal organs, being favored by a condition of deep anesthesia. Such an atony is comparable to the similar condition of the bladder which may follow operations about the perineum, or to the stopping of the frog's heart in diastole as the result of light tapping on the abdominal wall. An extreme degree of gastric dilatation may occur in the course of acute peritonitis. In such a case the atony is probably due to the direct action of toxins on the nervous mechanism of the stomach.

Atony itself, however, will not adequately account for the condition. The actual distension is produced in the operation cases by

gas, in the non-operation cases by fluid or food where the patient literally eats himself into the condition. Where does this gas come from? Its exact origin cannot be proved, but it is probable that in most cases it is the result of air-swallowing by the patient whilst under anesthesia. In some cases which have developed during the course of an operation, passage of the stomach tube with liberation of the gas has been followed by an immediate collapse of the distended stomach, only to be succeeded by a rapid reaccumulation of gas due to air-swallowing. In the later stages the great outpouring of fluid, the so-called gastric succorrhea, doubtless plays an important part in the maintenance of the distension.

Acute dilatation of the stomach is a condition of extreme gravity, and likely to prove fatal unless diagnosed early and treated with promptness. Operative treatment has been entirely replaced by the use of the stomach tube and the prone position.

CHRONIC DUODENAL ILEUS

A condition which is attracting more and more attention is chronic duodenal ileus from compression of the third part of the duodenum

FIG. 96.—Enormous dilatation of stomach and duodenum. The duodenum was obstructed by the root of the mesentery.

by the root of the mesentery. Even in a normal subject the third part of the duodenum is compressed and narrowed as it passes under the root of the mesentery.

It follows that some degree of obstruction may result if the angle through which the duodenum passes between the superior mesenteric artery and the aorta becomes narrowed. Anything which produces a drag on the intestines may lead to this result. Two factors in particular may be mentioned: (1) Where the empty small intestine

hangs over the pelvic brim but without resting on the floor of the pelvis when the patient is in an upright position; (2) Where the cecum and ascending colon prolapse into the pelvis, owing to congenital lack of fixation, and exert traction in the line of the mesenteric vessels.

The duodenum may be enormously dilated, as is well shown in a specimen in the Pathological Museum of the University of Manitoba (Fig. 96). The pylorus usually shares in this dilatation. The dilatation ceases abruptly at the point where the mesenteric vessels cross the bowel. The wall may be considerably thickened. The remainder of the small intestine is empty and collapsed. When the condition is detected at operation, and the root of the mesentery lifted up by a finger passed behind it, the duodenal contents will pass on into the jejunum.

The condition is associated with chronic dyspepsia, which is often relieved by the patient lying on his face. Walking and standing naturally aggravate the symptoms. Periodic, so-called, bilious attacks are frequent. Wilkie suggests that many cases of acute dilatation of the stomach may be merely a gross manifestation of a previously present chronic condition.

HOUR-GLASS STOMACH

In this condition the stomach is divided into two compartments, of which the pyloric is usually the smaller of the two. It may however be as large as the cardiac half, in which cases there is danger of mistaking it for the whole stomach.

The chief causes are: (1) a "saddle-shaped" ulcer on the lesser curvature extending on to both anterior and posterior walls, and pulling up the greater curvature in the process of contraction, (2) perigastric adhesions, (3) carcinoma, (4) a congenital condition—very rare.

DUODENAL DIVERTICULA

Although the condition of diverticulum of the duodenum was described as long ago as 1710, its frequency has only been recognized as the result of recent X-ray studies. Some roentgenologists report the incidence as high as 1 or 2 per cent of the cases which they examine.

The diverticulum varies in size from that of a pea to that of a small pear. In the larger specimens the opening is quite narrow. As in duodenal carcinoma, the common site is the second portion of the duodenum in the neighborhood of the ampulla of Vater, then comes the first, and lastly the third portion. The diverticulum springs from the inner and posterior aspect of the bowel along the line of entrance of the vessels, a line of weakness where in other parts of the intestine, particularly the appendix, fat may be seen entering the wall and reaching the submucosa. Although usually single the diverticula may be multiple. Like aneurism, it occurs in middle and later life. Rare cases, however, have been reported in infants.

The condition is in the nature of an aneurism. The mucosa and muscularis mucosæ are protruded through the muscular wall, so that the wall of the sac is formed by these structures alone. The causes, therefore, although obscure and probably complex, are akin to those responsible for the production of an aneurism. Of these the two most important are weakening of the wall and increase of pressure within the bowel.

The weakness of the wall may be a congenital defect; it may be associated, in the case of the first part of the duodenum, with the presence of an ulcer; it may be due to traction from without from gall bladder disease; or it may be traced to the presence of rests of pancreatic tissue which are not infrequently found in the wall of the sac. The increase of pressure is attributed by Keith to enteroptosis and partial obstruction at the duodenojejunal junction.

Whilst usually discovered accidentally, the diverticulum may occasionally be accompanied by gastric symptoms, and when large may even give rise to obstruction.

RARE CONDITIONS

Pyloric stenosis of infants is a condition in which there is great obstruction at the pylorus in early life. It used to be thought that there was a congenital overgrowth of muscle at the pylorus, but it is now believed to be more probably secondary to pyloric spasm.

The stomach is distended and the walls are thickened. There is extreme thickening of the circular muscle at the pylorus, which is responsible for a marked degree of obstruction.

Congenital stricture of the duodenum is a rare condition in which the duodenum is closed off, usually at the point of entrance of the common bile duct. The proximal part becomes greatly dilated.

Foreign Bodies.—Apart from small objects which may be swallowed accidentally, the most important foreign body is the "hair-ball." This is found principally in insane female patients, who chew and swallow the hair until a mass which may weigh as much as 5 lbs. is formed in the stomach.

Innocent tumors are uncommon. Fibroma, myoma, and fibromyoma may grow in the muscular wall. Lipomata may occur under the serous coat, and an adenomatous polypus may project into the cavity.

Sarcoma of the stomach is of equal frequency in men and women. It is usually of the round-celled variety, but may be spindle-celled. It starts in the submucous coat, and may attain an enormous size, bulging into the cavity, or growing outwards to form a mass outside the stomach. Recently I performed an autopsy on a case which had been diagnosed as cancer of the lower end of the esophagus.

Tuberculosis may be primary or secondary to a lesion in the lung. It occurs in two forms: (1) as a tuberculous ulcer of the body of the stomach, (2) as a hypertrophic condition at the pylorus which may be mistaken for carcinoma.

Syphilis of the Stomach.—Although it has been the custom to regard syphilis of the stomach as a pathological rarity, the recent work of Smithies, Eusterman, and others suggests that it may be commoner than has been suspected.

The diagnosis is always a difficult matter. A positive Wassermann reaction does not indicate that the gastric lesion is syphilitic, nor does a negative reaction exclude the possibility of syphilis. The cases may be arranged in three clinical groups: (1) those which resemble gastric ulcer, (2) those which resemble gastric carcinoma; and (3) atypical cases. The condition of the stomach contents usually suggests carcinoma, for the acidity is low and blood may be present.

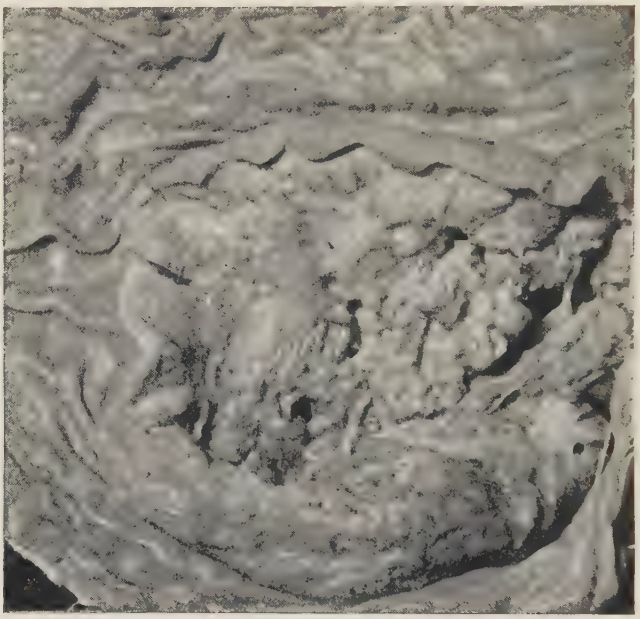

FIG. 97.—Huge sarcomatous ulcer of stomach.

The pathology is merely that of tertiary syphilis. The spirochetes settle down in the stomach, chiefly in the submucosa, and the inflammatory reaction which they call forth leads to the production of miliary gummata. The disease may follow three main lines: (1) the gumma may ulcerate and produce a gastric ulcer; (2) a large mass suggestive of a carcinoma may be formed in the stomach wall; or (3) there may be a diffuse infiltration with fibrosis. The first of these forms will therefore simulate gastric ulcer, the second will simulate the bulky variety of carcinoma of the stomach, whilst the third is apt to be mistaken for a diffuse scirrhous growth or linitis plastica. Even at operation a correct differentiation may be impossible. In the late stages healing may occur with cicatrization, contraction, and stenosis. One feature of the syphilitic ulcer is that not infrequently it is multiple.

The *microscopic appearance* is just what might be expected. In the early stages there are nodular collections of lymphocytes and plasma cells, endarteritis obliterans, and periarteritis. Later there may be necrosis, or the formation of dense scar tissue. The mucosa is atrophied or ulcerated, whilst the submucosa and muscularis are thickened and fibrosed.

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CHAPTER XVII

THE INTESTINES

In this chapter the more important pathological conditions affecting the intestine will be considered. The duodenum, the vermiform appendix, and the rectum are not included, the former having already been considered in connection with the stomach, and the two latter having special chapters devoted to them.

The surgical diseases of the intestines are many and varied, and it is difficult to group them into any convenient classification. They may, however, be considered under the following headings: (1) intestinal obstruction, (2) inflammations, and (3) tumors.

INTESTINAL OBSTRUCTION: ILEUS

The intestine is a hollow muscular tube the functions of which are the digestion of the food stuffs, their absorption after digestion, and the conveyance of unabsorbed matter to the rectum for expulsion from the body. The passage of the food along the tube is dependent on the muscular contractions of the bowel. These are of two varieties. (1) Rythmic segmentation, a series of contractions by which the bowel is divided into a number of segments, which are at once broken up into other segments, so that the food is thoroughly mixed with the digestive juices without changing its position in the bowel. (2) Peristalsis, whereby the food is caused to move along the bowel, owing to contraction of the part immediately above the mass and dilatation of the part immediately below.

It is obvious that where obstruction of the bowel occurs from any cause these movements will be seriously interfered with. The peristaltic movements may become violent in their endeavor to force the contents past the obstruction, and the severe pain of intestinal colic will be felt. It is not yet certain whether this pain is felt in the bowel wall or is "referred pain" felt in the parietes. Normally the visceral peritoneum is insensitive, whereas the parietal peritoneum is exquisitely sensitive. The pain of early appendicitis is referred to the abdominal wall in the region of the umbilicus, as is that felt in strangulation of the small intestine. Whether the pain is referred in every case of intestinal disorder we cannot yet say.

There are many different classifications of intestinal obstruction, for which the reader is referred to Sir Frederick Treves' classical work. It is enough here to recognize two main divisions, the paralytic and the mechanical. In the *paralytic form* the intestinal tube is unable to pass on its contents, and the obstruction is as effective as if the

lumen were blocked. The commonest and most important cause of intestinal paralysis is diffuse or localized acute inflammation. The *mechanical variety* may be due to a number of obstructive causes which will be taken up presently.

The term ileus is often used in place of obstruction. Ileus literally means a twist, but it has come to mean any condition in which the onward flow of intestinal contents is impeded.

Intestinal obstruction may be acute or chronic. The former comes on with dramatic suddenness, sometimes with the rapidity of lightning, whilst the approach of the latter is gradual and insidious. Frequently, however, in the last stages the chronic form suddenly becomes acute. The fundamental difference between the two forms is that in the acute variety the blood and nerve supply to the bowel is cut off, in the chronic it is not.

Acute Obstruction.—Sudden obstruction may be caused by a number of factors discussed presently. One of the most common causes is strangulation of an intestinal hernia by a fibrous band. The strangulation is usually tight enough to obstruct the veins but not the arteries.

The bowel below the obstruction soon empties, and remains pale and contracted. The part above the obstruction presents a very different appearance. It rapidly becomes distended with fluid poured out from the intestinal wall, and with gas which the occluded veins are unable to absorb. The wall becomes deeply congested, cyanotic, purple, or almost black in color, for blood continues to flow in through the patent arteries but cannot escape owing to the venous obstruction. The mucous membrane becomes necrosed, and numerous small ulcers are formed, through which bacteria pass to give rise to general peritoneal infection. In cases in which the arteries are occluded from the beginning the color of the wall is pale green, rapidly passing into the dark green of gangrene.

The *symptoms* of acute obstruction belong to two groups. (1) There is pain, vomiting, and shock, due to trauma to the sympathetic nervous system. (2) Soon these are followed by even more serious symptoms of toxic absorption, such as collapse, subnormal temperature, muscular relaxation, with a weak and rapid pulse.

Wilkie has shown very conclusively by experiments on cats that the earlier symptoms are not due to the absorption of toxic products, but to shock with its associated splanchnic paresis and loss of fluid from the circulation either into the bowel by or vomiting. Death in the early stages is not from peritonitis, which does not play an important part until after 24 hours.

Whipple's experiments on closed duodenal loops in dogs throw much light on these later symptoms. When a loop of bowel is tied off it is soon found to contain highly toxic substances, of the nature of proteoses, which when injected intravenously into normal dogs produce severe intestinal congestion, diarrhea, vomiting, and collapse. Whipple

considers that the poison is formed from the epithelium of the bowel, rather than from the contents of the loop. This substance cannot be obtained from normal duodenal mucous membrane, obstruction being an essential factor.

The work of Davis and Stone throws doubt upon this explanation. They found that the secretion of the normal intestine was non-toxic, and that it remained so when kept under conditions which prevented bacterial growth. When, however, it was incubated it developed within 18 hours markedly toxic properties, and on injection produced symptoms like those of fluid from closed intestinal loops. The toxic substance is apparently not due, as at first supposed, to the action of bacteria on the intestinal mucosa with the production of necrosis, but rather to the splitting up of some substance in the intestinal contents by bacterial action.

The exact nature of the toxic substance is still a matter of dispute, but it is probably a proteose or split protein derivative. We know from the work of Vaughan how intensely toxic such split proteins may be. It is a curious fact that the toxic contents of an intestinal loop which when injected intravenously produce such marked effects are without effect when injected into the normal bowel. It has been thought that the toxins are not absorbed through the normal mucosa, but it appears more probable, as suggested by Stone, that absorption does actually take place, but that the first effect is that noted in experimental injection, namely increase in the tone and peristalsis of the bowel, so that the toxic products are hurried out before they can be absorbed. In the obstructed bowel there is plenty of time for absorption. These experiments emphasize the extreme importance of early operation and evacuation of the contents of the obstructed portion of bowel. The lower down the obstruction is produced, the less toxic is the material formed. This corresponds with what is observed clinically, for a low obstruction is not nearly so disastrous in its consequences as that produced at a higher level.

Large quantities of indican are excreted in the urine, indicating that intestinal fermentation is active. Another striking feature is the very high non-protein nitrogen content of the blood, which may attain the same level as that found in uremic coma. Whipple and his associates have shown that this increase in the non-protein nitrogen of the blood is present in dogs in whom an intestinal loop has been tied off, and Rabinowitch at the Montreal General Hospital found high readings in intestinal obstruction, acute general peritonitis, and acute pancreatitis. The rise appears to be due to the increased tissue destruction from the toxic effect of the proteose absorbed. It is of great prognostic value, for when it is maintained the case is almost certainly progressing to an unfavorable termination.

A change of equal or perhaps even greater importance is that in the chlorides of the blood. Haden and Orr have shown both in experimental animals and in man that there is a marked fall in the blood chlorides when the upper intestinal tract is obstructed, together with

an alkalosis as evidenced by the high carbon dioxide combining power of the plasma. This is accompanied by a diminished excretion of chlorides in the urine; indeed so marked may be the chloride retention that the urinary chlorides may almost completely disappear. Administration of sodium chloride by the mouth, by the rectum, or by hypodermoclysis causes the blood chlorides to rise to normal again, together with a corresponding fall in the non-protein nitrogen, and a remarkable and rapid improvement in the condition of the patient, so much so indeed that the risk of operation may be very greatly reduced. Haden and Orr suggest that the chloride ion reacts with the toxin in some way so as to detoxicate it and thus produce some harmless inert substance. The action is specific for sodium chloride; other chlorides produce no benefit, and water by itself actually increases the intoxication. Cameron, of the University of Manitoba, has shown that a marked chloride retention may be induced by injecting dogs with the soluble absorbable non-protein poisons of a toxic brew of digested meat which has been infected with intestinal bacteria. He has also confirmed the observation of Cori and Pucher that a similar chloride retention may be produced as a result of deep X-ray therapy applied to the epigastrium.

Chronic Obstruction.—This variety differs from the acute form in two important particulars: (1) the obstruction comes on slowly and insidiously, and (2) there is no interference with the vascular and nervous supply of the part. The obstruction may be due to the growth of a tumor (usually a carcinoma) in the wall of the bowel, to the gradual contraction of a band of scar tissue, or to pressure from without.

The effects of the obstruction on the bowel are those which might have been expected and foretold. Below the obstruction the bowel is collapsed and empty. Above, a varying degree of dilatation and hypertrophy takes place, hypertrophy especially in the small intestine, dilatation in the large. If the obstruction be *partial* hypertrophy is marked, owing to the active efforts of the bowel to force the intestinal contents past the obstruction. If it be *complete* the muscular contractions cease, there is paresis of the muscular coat, and the bowel above the obstruction undergoes passive dilatation. In the first case the result is a small cavity with thick walls, in the second a large cavity with thin walls. These principles may be applied to obstruction of any of the hollow viscera, the stomach, the intestine, the gall bladder, and the urinary bladder.

The distended bowel separates the two layers of the mesentery, so that shortening of the mesentery occurs, with fixation of the bowel.

So-called stercoral ulcers of the mucous membrane develop in the segment above the obstruction, owing to the irritation of the hard scyballous masses which collect there. A certain amount of catarrhal inflammation develops in consequence, with the result that there may be periodic attacks of diarrhea with the passage of semi-fluid matter mixed with mucus. Attacks of diarrhea alternating with periods of constipation are thus always highly suggestive of chronic obstruction.

The common causes of intestinal obstruction, acute or chronic, are (1) carcinoma; (2) adhesions, bands, and cicatrices; and (3) inversions and torsions.

CARCINOMA

The common sites of cancer of the bowel, when the rectum is excluded, are the cecum and the pelvic colon. The next most frequent positions are the ascending colon, the splenic flexure, and the hepatic flexure. Cancer of the small intestine is of very rare occurrence.

The growth commences in the mucous membrane as an adenocarcinoma. The appearance varies with the mode of growth. (1)

Fig. 98.—Carcinoma of bowel of the fungating type.

The tumor may project into the lumen as a fungating, cauliflower-like mass which speedily becomes ulcerated, with the usual addition of symptoms of toxemia to the clinical picture. The typical microscopic appearance of adenocarcinoma is well maintained.

Or (2) the carcinoma may infiltrate the bowel wall rather than project into the lumen. An annular growth is formed round the

gut, which is comparatively poor in epithelial elements but rich in fibrous tissue, so that the tumor is a scirrhus such as has already been studied in the pylorus of the stomach. The contraction of the fibrous tissue causes narrowing of the lumen much more extreme than that produced by the previous variety; and in many cases it looks as if a tight string had been tied around the bowel, the actual tumor being of quite small dimensions. In this form ulceration is of comparatively late date.

In both forms colloid degeneration is not uncommon. Indeed it is more frequent in the intestine than in the stomach. Care must be

FIG. 99.—Carcinoma of large intestine, with extreme dilatation above the obstruction.

taken not to make a mistake in the microscopic diagnosis, for in some sections the appearance may be merely that of mucoid degeneration, not an epithelial cell being visible.

Cancer of the bowel cannot be considered one of the highly malignant forms of carcinoma, for involvement of the mesenteric and retroperitoneal glands occurs somewhat late, and metastatic growth in the liver through the portal stream is also a late occurrence. Adhesions

to the surrounding parts may occur, and the carcinoma cells may penetrate the serous coat and give rise to secondary nodules on the peritoneum and the pelvic organs, such as the ovaries. On the whole the prognosis is good, provided the diagnosis is made reasonably early.

ADHESIONS, BANDS, AND CICATRICES

There is a multiplicity of ways in which bands in the abdomen may cause strangulation of the bowel.

In an *ordinary hernia* an additional knuckle of bowel may slip through the inguinal or femoral ring, and become constricted by the unyielding margin of the ring. Or a *retroperitoneal hernia* may occur into one of the peritoneal pouches, of which the principal are the *paraduodenal fossa*, situated on the left side of the ascending part of the duodenum with its left border formed by the inferior mesenteric vein; the *mesenterico-parietal fossa*, of which the anterior boundary is formed by the superior mesenteric artery; the fossæ in the neighborhood of the *ileo-cecal* junction, notably the *ileo-appendicular* and the *retrocolic;* and in rare cases there may be a hernia into the foramen of Winslow and other unusual sites.

Peritoneal adhesions are a not uncommon cause of intestinal obstruction. Owing to some previous attack of inflammation a fibrous band is formed which stretches from the wall of the bowel to some fixed point, and by gradual contraction may pull upon the bowel to such an extent as to produce kinking and obstruction. In these cases there is no sudden obstruction to the blood supply of the part, and the symptoms are therefore less catastrophic in nature.

Obstruction may be produced by abnormal bands of peritoneum or omentum, by a *Meckel's diverticulum*, or by an *appendix* or *Fallopian tube* which has become adherent to the parietes.

INVERSIONS AND TORSIONS

Intussusception.—Rutherford Morison remarks that the tendency to turn inside-out seems common to all of the hollow viscera. It is most frequently met with in the intestine, and at least 75 per cent of the cases occur within the first year. Of these about 70 per cent are in boys.

The effect of intussusception depends on whether there is interference with the blood supply. If there is, the symptoms will be those of acute obstruction and strangulation; this is what usually occurs. If there is not, the condition is more or less chronic.

By far the commonest position is the ileo-cecal junction. This is because local inflammation and other sources of irritation are common in this position, and the disparity in size between the small and the large intestine favors the production of the condition. The inversion may occur at other parts of the bowel, especially if a polypus happens to be projecting into the lumen. Indeed innocent tumors of the bowel derive much of their importance from their tendency to predispose to this accident.

The muscular contractions of the sheath soon produce venous congestion and swelling of the contained part, the two layers of which become adherent to one another owing to the inflammation which rapidly supervenes. Blood is effused into the wall and lumen of the bowel, and is discharged, mixed with mucus, from the rectum.

As the intussusception progresses along the large intestine it assumes a curved, sausage-shaped appearance, owing to the traction of the mesentery attached to the promontory of the sacrum. Twisting

Fig. 100.—Intussusception at ileo-cecal junction.

of the mesentery is naturally liable to occur, in which case symptoms of acute strangulation rapidly supervene. Bacteria invade the walls of the bowel, so that gangrene is the next step. This involves the entering and returning portions, but seldom the sheath. The prognosis depends entirely on the rapidity with which a correct diagnosis is made and appropriate treatment carried out.

In the course of an autopsy small intussusceptions, frequently multiple, are often observed in the small intestine. These are agonal in nature, being produced by the irregular spasmodic contractions

at the time of death. They are readily recognized through presenting no signs of inflammation, and being readily reduced.

Volvulus.—Torsion is an accident to which many of the abdominal organs are liable—the intestine, the gall-bladder, the kidney, the spleen, the testicle, the uterus (especially when the seat of fibroids), an ovarian cyst, a hydrosalpinx or pyosalpinx, etc. Of these torsion of an ovarian tumor is the commonest, whilst the intestine comes next in frequency.

The causes of volvulus are obscure. Chronic constipation and congenital or acquired defects in the mesenteric attachment probably play an important part. The actual twisting may be brought about by irregular peristaltic contractions, or a physical factor such as the weight of the distended bowel may be the exciting cause. The pelvic colon is much the commonest site of the accident.

The result of the twisting is to produce strangulation and acute obstruction, owing to occlusion of the vessels in the mesenteric attachment, first the veins and then the arteries. The effect is first extreme venous engorgement, and then gangrene of the bowel.

INFLAMMATORY CONDITIONS

The intestine may be the seat of a variety of inflammatory affections. Of these the most important are tuberculosis, typhoid fever, dysentery, and fibromatosis of the colon. Secondary inflammations, such for instance as the stercoral ulcers produced by accumulations of fecal masses, have already been considered. The lesions of typhoid and dysentery are more properly discussed in works on medicine. Tuberculosis and the chronic inflammatory condition known as fibromatosis will be taken up here.

Tuberculosis of the Intestine

Tuberculosis of the bowel occurs in two forms which are so distinct from one another that they will be described separately. These are (1) the ulcerative variety, (2) the hypertrophic variety.

Ulcerative Tuberculosis.—Ulceration of the bowel due to tuberculosis usually occurs in children or in young adults. The common site is the lower end of the ileum, but the ulcers may be scattered over a considerable length of bowel, involving either the lower end of the small intestine or the commencement of the large intestine, or both.

This, at least, is the result of pathological investigation conducted in the autopsy room. Recently, however, the ulcerative variety of intestinal tuberculosis has been attracting the attention of surgeons, and the findings of the operating room differ somewhat from those of the autopsy room. In the former the early stages are seen, in the latter only the end picture. The work of Archibald and others has shown that the disease commences in the cecum, and spreads from there both up and down the bowel. This progress was well seen in a number of cases in which a second laparotomy was done some months later. In the majority of Archibald's cases the cecum was easy to palpate,

whether the small bowel or the rest of the colon was involved or not. The remainder of the colon may show isolated ulcers, but is rarely involved so extensively as to be palpable. The limits of the disease can be recognized at operation from the tell-tale signs enumerated below.

The infection may be primary, due to ingestion of the bacilli in tuberculous milk, a method common enough in children but very rare in adults; or it may be secondary, due to the swallowing of tuberculous sputum.

The lymphoid tissue in the Peyer's patches and solitary glands is the first to be infected, but the disease differs from typhoid in that it does not remain confined to these structures, but spreads along the wall of the bowel, often in an encircling manner so as to give rise to "girdle ulcers." The edges of the ulcers are ragged, irregular, and often under-

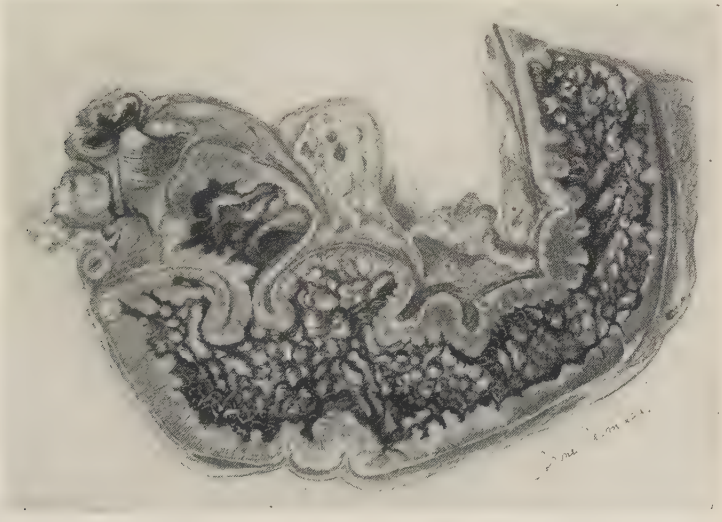

Fig. 101.—Hypertrophic tuberculosis of cecum.

mined, whilst the floor is covered with small tubercles. The position and nature of the ulcers can be recognized from the outside, the wall is thickened and the peritoneal coat congested at the spot, and minute grey tubercles or a patch of reactive fibrino-plastic exudate may betray the position of the underlying ulcer. Enlargement of the lymphatic glands, with or without caseation, is common.

Adhesions to surrounding parts are common, and this together with the inflammatory thickening of the serous coat which is commonly present, renders perforation an uncommon accident.

The great surgical importance of ulcerative tuberculosis lies in the fact that healing is followed by cicatricial contraction which, on account of the encircling form of the ulcer, may give rise to a marked degree of obstruction. As the ulcers are often multiple, there may be

several points of stricture, the intervening segments showing a dilatation and sacculation which is quite characteristic.

Hypertrophic Tuberculosis.—In this condition the formative are in excess of the destructive processes. It always commences in the ileocecal region, although it may spread upwards along the ileum and downwards along the cecum. It occurs in young adults, and is rare over the age of forty.

There is a great formation of tuberculous granulation tissue, similar to that which is found in tuberculous synovial membranes, mainly in the submucous but to some extent also in the subperitoneal coat. Giant cells are abundant but miliary tubercles are not common, and caseation is usually absent.

Owing to the formation of new tissue in the submucosa, the mucous membrane is folded and nodular, and projects into the lumen in the form of small papillomatous masses. Ulceration may develop, but is not a marked feature of the condition. The mucosa may gradually encroach upon the lumen until extreme narrowing results, so that it may only be possible to pass a fine probe through the opening.

The affected part of the bowel is thickened and stiff, and may form a tumor-like mass which may bear a strong resemblance to a carcinoma even after the abdomen has been opened. The neighboring lymphatic glands are usually enlarged, thus still further adding to the mass which is felt through the abdominal wall. The more diffuse nature of the thickening and the younger age of the patient are points in the differentiation from carcinoma.

Fibromatosis of the Colon

This is a condition which closely simulates the hypertrophic form of tuberculosis, both in its morbid anatomy and its clinical manifestations. It is often mistaken for the hypertrophic form of intestinal tuberculosis or for malignant disease. Indeed it is probable that many cases which have been diagnosed as carcinoma on the operating table and have cleared up after colostomy were in reality examples of fibromatosis. In this it resembles another chronic inflammatory condition affecting the same region, namely diverticulitis.

Although it may affect any part of the large intestine it is commonest in the pelvic colon and the rectum. The wall of the bowel for a varying distance is thickened owing to the formation of dense inflammatory tissue in the submucous coat. The mucosa is nodular or polypoid as in tuberculosis, and may be ulcerated. In one specimen removed at operation which I studied, the mucosa was thrown into a remarkable series of stiff ridges, and the fibrosis was extreme, although comparatively few inflammatory cells could be found.

The exact cause of the condition is not known, but it is evidently chronic inflammatory in nature. The infection probably gains access to the submucosa through the mucous membrane by some abrasion or other local lesion.

FECAL FISTULA

A fecal fistula is an abnormal track by means of which the lumen of the bowel communicates with the surface of the skin. It may be due to many causes, of which the chief are (1) perforating wounds of the abdomen and (2) the development of an abscess which establishes a communication between the bowel and the skin.

The length of the fistula depends on whether the bowel has become adherent to the abdominal wall before the formation of the fistula. Suppuration in the neighborhood of the appendix is one of the commonest causes. In such a case the fistulous track will be lined by granulation tissue, and pus will be present in the discharge. In one of our cases perforation of the bowel with the establishment of a fistula was due to pressure from a rubber drainage tube.

The part of the bowel involved may be indicated by the nature of the discharge. If the latter is acid in reaction, contains bile and undigested food, and produces irritation of the skin, the upper part of the jejunum is probably involved. If it is alkaline in reaction, and contains no recognizable bile or undigested food, the opening is probably into the lower part of the small intestine. If it is fecal in odor, semi-fluid in consistence, and contains mucus, the fistula communicates with the cecum. If the contents are almost solid and evidently fecal, the lower part of the colon is implicated.

INTESTINAL DIVERTICULA

Of late years much attention has been paid to the occurrence of diverticula of the intestine. These are most commonly found in the large intestine, particularly the descending colon and the sigmoid. The site of election, indeed, is the sigmoid, and for practical purposes diverticula of the large intestine may be regarded as diverticula of the sigmoid. The diverticula, even though present in great numbers, almost always stop abruptly at the line of junction between sigmoid and rectum. Their abundance in the sigmoid is probably due to the accumulation of feces and the frequent presence of gas in that part, whilst their absence in the rectum may be attributed to the lack of appendices epiploicæ there, and to the fact that the longitudinal muscular bands (tenia coli) disappear in the rectum, the fibers being diffused over the entire rectal wall, thus lending it additional strength. They may be noticed in the course of an autopsy, having given rise to no symptoms. Very often, however, they are the cause of symptoms of varying degrees of severity.

It may appear a matter for wonder that diverticula, which are now encountered with comparative frequency, should have been so completely overlooked in the past, even by morbid anatomists of wide experience. The reason is two-fold; (1) the diverticula are small and are usually buried in fat; (2) the secondary pathological changes presently to be described tend even more effectually to cover up the diverticula.

The diverticula may occur at any period of life, but they are more common in middle and late life. They are extremely rare before the age of thirty. In the small intestine they are almost invariably situated along the mesenteric border, and, being empty of feces, seldom give rise to any symptoms. In the large intestine they usually bear no relation to the mesentery, but adjoin the appendices epiploicæ, and commonly give rise to symptoms which may be mild or severe.

The average *size* of the diverticula is that of a large pea, but they vary from microscopic dimensions up to the size of a plum stone. The greater number are sessile, but some may be pedunculated. The opening into the intestinal lumen varies much in diameter; in some cases the opening is so small as to constitute a real stenosis. The *contents* consist of fecal matter; hard concretions may be

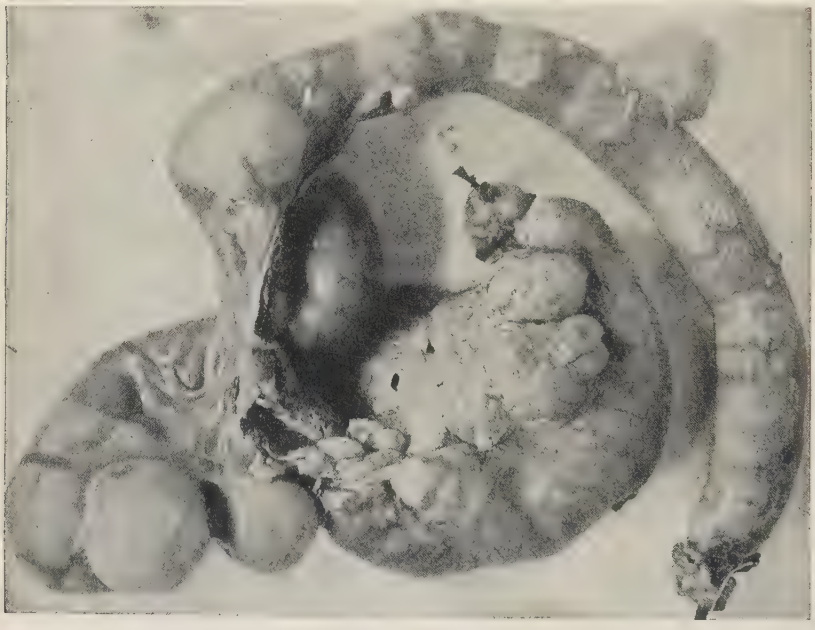

Fig. 102.—Hodenpyl's specimen of multiple acquired diverticula of the colon (sigmoid flexure). (Brewer.)

present. In the small intestine the contents are fluid. There can be little doubt that the difference in the contents of the diverticula explains why the lesion in the small intestine should almost never be accompanied by symptoms, whilst in the large intestine pathological complications are frequent.

The diverticula are sometimes divided into the congenital and the acquired. It is probable that the acquired depend upon an original congenital weakness of the intestinal wall. The congenital class is due to some embryological defect; Meckel's diverticulum is a good example.

Another subdivision is into the complete and the incomplete. In the complete the sac is formed of all the layers of the intestinal wall. In the incomplete or false diverticula, which are by far the commoner, the sac is formed of mucosa, submucosa, and serosa. It is indeed a hernia mucosæ through a weak point in the muscular coat.

Etiology.—The etiology of diverticula formation is not certain, but McGrath, as the result of a combined anatomical and experimental investigation, came to the following conclusions. No single factor explains the origin of the ordinary form of diverticula. As in the case of an aneurism or an ordinary hernia the fundamental factors are insufficient resistance of the wall and increased pressure from within. The weakening of the wall may be congenital in origin, it may be due to general degenerative changes, debilitating disease, and senility, or it may arise in local conditions such as chronic constipation.

In the small intestine the diverticula occur along the line of the mesenteric attachment, because it is at this point that the vessels pierce the bowel wall, often carrying in with them a sheath of fat, and thereby constituting a *locus minoris resistentiæ*. In the large intestine on the other hand, they are situated along the convexity rather than the concavity of the gut, frequently in two rows, and almost always multiple. The hernial protrusion of mucosa most commonly takes place into the appendices epiploicæ, for these, being frequently filled with fat, are areas of lessened resistance.

Diverticulitis.—Infection may lead to an inflammatory condition of diverticulitis which may be either acute or chronic. The *acute changes* are quite analogous to what is seen in the appendix. As the result of the presence of a hard concretion irritation is set up, the effect of which may vary from a slight abrasion of the mucosa to perforation resulting in general peritonitis, local abscess formation, or fistulous communication with other viscera or with the abdominal wall. Perforation of a diverticulum is a comparatively frequent occurrence, and may be the first indication that there is anything amiss. Often, however, the surrounding adhesions are sufficient to ensure that the perforation will do no more than result in a local abscess. The symptoms may naturally closely simulate those of acute appendicitis, except that the lesion is on the left side of the abdomen.

Equally important are the *chronic results* of infection, to which Wilson has given the name of *peridiverticulitis*. This is a condition of chronic extramucosal inflammation, the result of a leakage of toxins or bacteria through the mucosa, with the formation of a large mass and not infrequently the production of stenosis. It is obvious how readily such a condition may be mistaken for carcinoma. Even at operation the mistake is readily made, for the diverticula are completely buried in the dense inflammatory mass.

Many of the cases of spontaneous cure of cancer of the sigmoid, with or without the aid of Christian Science, were doubtless examples of this condition. In his excellent paper on the subject Telling remarks: "Of all the secondary results this proliferative inflammation

is the most important, the most frequent, and probably the most overlooked." The resected mass consists of a large amount of fat and dense fibrous tissue. Microscopically it is made up of granulation tissue containing an abundance of the fixed connective tissue cells. Giant cells may be met with, and these must not give rise to a mistaken diagnosis of tuberculosis. When the lumen is opened the mucosa is found to be intact, but small pits with edematous margins are seen; these are the openings of the diverticula into which a probe may be passed. In order best to demonstrate the diverticula McGrath recommends that thin slices should be cut from the external surface of the mass; when the opening of a diverticulum is encountered a probe can be passed into the lumen of the bowel.

Fig. 103.—Peridiverticulitis. Sketch of diverticulum with inflammatory deposit in subserosa. (W. J. Mayo, Wilson, and Giffin.)

Relation to Carcinoma.—A feature of great importance is the occasional development of carcinoma in conjunction with diverticulitis. Among 42 cases which W. J. Mayo resected for diverticulitis in 3 he found carcinoma present. This appears to be another example of the relation of chronic irritation to the production of carcinoma. A simple method of differentiating in the gross between carcinoma, and diverticulitis has evidently been usually overlooked in the past, considering how frequently diverticulitis has been mistaken for carcinoma, and that specimens of the former disease have even found their way into museums labelled as the latter. In diverticulitis there is practically never any ulceration or involvement of the mucous membrane; in carcinoma this is extremely frequent.

Meckel's Diverticulum.—The vitelline duct or yolk stalk which connects the yolk sack with the intestine is obliterated early in intrauterine life and the fibrous cord into which it is converted becomes incorporated with the umbilical cord, so that it passes to the umbilicus.

In about 3 per cent of cases that part of the yolk stalk which lies between the intestine and the umbilicus fails to degenerate, and remains patent. As a rule it is only the proximal part which remains open. This forms a pouch-like projection which arises from the lower end of the ileum, usually within two feet of the ileo-cecal junction. The projection may be a mere dimple, or it may extend as far as the umbilicus, thus forming an umbilical fistula through which feces may escape. The pouch

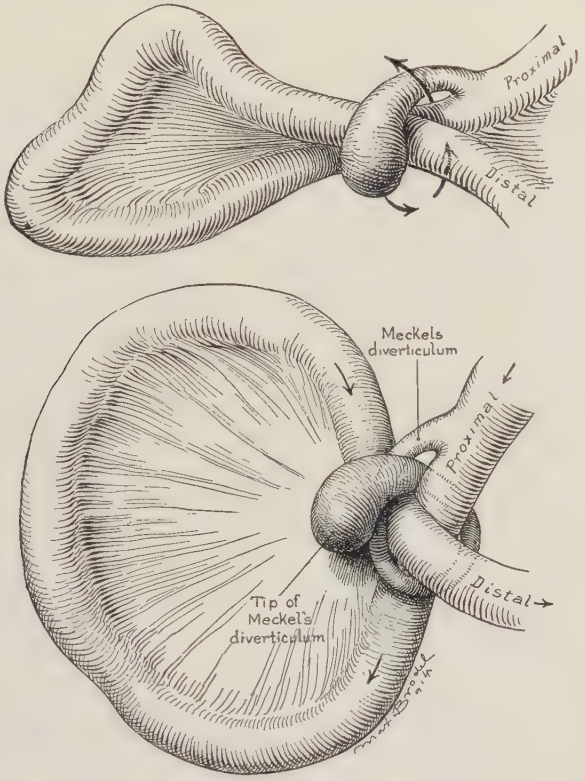

FIG. 104.—A diverticulum tying off a loop of small bowel. This indicates the manner in which the obstruction occurred. Meckel's diverticulum has dropped over a loop of bowel which has been partly twisted. After passing under the loop it curves upward and passes through the space between the base of the diverticulum and the adjacent small bowel. With the consequent distention of the constricted bowel, complete obstruction has resulted. (Cullen.)

is generally quite short, is continued as a fibrous band which may be adherent to the umbilicus, or may form some new attachment to the mesentery of the ileum or a loop of intestine. The surgical importance of the condition lies in the danger of such a band giving rise to strangulation of a loop of bowel which may be forced over or under it.

One very curious anomaly of development in this region came under my notice recently. A newly-born child developed symptoms of

complete intestinal obstruction, and died on the ninth day. At the autopsy a fibrous band extended from the lower end of the ileum to the umbilicus. The terminal portion of the ileum was completely obliterated and converted into a fibrous cord 3½ inches long, which was joined at right angles by the cord from the umbilicus. Such a congenital obliteration of the bowel is of very rare occurrence. About one third of the recorded cases have been in the duodenum, the remainder occurring throughout the small intestine. The lumen of the duodenum is normally obliterated by an overgrowth of mucous membrane for a brief period in a very early stage of development, and it may be that

Fig. 105.—Meckel's diverticulum associated with atresia of the lower part of the ileum.

the congenital closure represents a persistence of the early embryonic condition. Whether or not stenosis elsewhere in the small intestine is susceptible of a similar explanation, or whether it should be attributed to some inflammatory condition it is impossible to say.

HIRSCHSPRUNG'S DISEASE

Idiopathic dilatation of the colon or Hirschsprung's disease is a congenital condition of uncertain nature. The pelvic colon, and sometimes the descending colon, are enormously dilated and hypertrophied. The small intestine is normal. The hypertrophy is due to extreme thickening of the circular muscular coat. The mucosa shows some infiltration with inflammatory cells, and may become ulcerated

owing to the accumulation of scyballous masses. The submucosa is fibrous, and there is round-celled infiltration around the vessels.

Wilkie suggests that the condition originates at the time of birth, when the pelvic colon, which possesses a long and lax mesentery, is distended with meconium. If it fails to expel the meconium, owing to muscular weakness, the loop may sag downwards into the pelvis and become kinked, with the result that a condition of gradually increasing dilatation develops accompanied more or less by a corresponding hypertrophy of the muscular wall. This may not be a very satisfying explanation, but the same may be said of the score or so of other theories which have been advanced to explain the condition. It is fairly certain that dilatation precedes the hypertrophy, and the relation of the one to the other probably depends on the degree of obstruction which may be present.

FOREIGN BODIES

The two chief varieties of foreign body met with in the intestine are gall-stones and enteroliths.

A *gall-stone* may grow in the gall-bladder to such a size that it is unable to pass along the cystic duct. In rare cases inflammatory adhesions may form between the gall bladder and the second part of the duodenum, and the stone may ulcerate through into the bowel. There it may be gripped by the circular muscular fibers, and give rise to one variety of acute obstruction.

It might be supposed on *a priori* grounds that rupture would more commonly occur into the transverse colon, and that the stone would be found in the large intestine. As a matter of fact in the great majority of cases the obstruction occurs in the small intestine. Moreover the obstruction usually occurs at the lower end of the small intestine. One might expect the stone especially when large, to produce such intense irritation that the bowel would grip it and impede its further progress, but such is usually not the case. In one example of the condition studied recently in the Winnipeg General Hospital the stone was one of the largest that I have ever seen. It was a pure cholesterin calculus, almost spherical, and about the size of a pigeon's egg, and yet it apparently produced no symptoms until it reached the lower end of the ileum, where it became impacted, caused acute obstruction, and was then successfully removed.

An *enterolith* consists of a mass of calcium and magnesium phosphate which forms in the bowel, or more commonly in some pocket or diverticulum. It acts as a local irritant, and may produce obstruction usually chronic but in some cases acute.

Tumors.—There is only one common tumor of the bowel, carcinoma of the large intestine. Carcinoma may occasionally occur in the small intestine, and presents the same characters as when it grows in the large bowel.

Sarcoma sometimes occurs in the small intestine, and still more rarely in the large.

Adenomas, fibromas, lipomas, and myomas when they occur in the small intestine are usually pedunculated. Their chief importance is that they may form the starting point of an intussusception.

Multiple adenomas of the large intestine are often present in enormous numbers. They may be sessile, but are often pedunculated. They are most common in the lower part of the bowel.

Fig. 106.—Sarcoma of the small intestine.

ACTINOMYCOSIS

Infection may occur from the swallowing of an infected grain of seed. The usual site is the cecum, but the pelvic colon may also be affected. The appearance is that typical of an infective granuloma, namely ulceration of the mucosa and great thickening of the wall of the bowel. Suppuration occurs, and the ray fungus may be found in the pus. It is but natural that the clinical diagnosis should be a matter of the greatest difficulty and even after the abdomen has been opened mistakes will often be made. The two conditions with which it is most likely to be confused are tuberculosis and malignant disease.

Embolism of the Superior Mesenteric Artery.—This condition has already been fully discussed on page 148.

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CHAPTER XVIII

THE VERMIFORM APPENDIX

The vermiform appendix holds rather a peculiar position in medical science. It is a small and somewhat insignificant organ, but so are other organs which are now known to be all-important to the animal economy, such organs as the pituitary, the parathyroids, and the adrenals. The appendix owes its position of eminence not, however, to its physiological importance, but to the extreme frequency with which it becomes the seat of pathological changes.

Anatomy.—The *position* of the appendix varies considerably. As a rule it springs from the inner and posterior aspect of the cecum about one inch from the ileo-cecal valve, and points upwards and to the left towards the spleen. It may be retrocecal in position, passing upwards behind the cecum and ascending colon. Such a position favors the localization of an appendicular abscess. Or it may hang down over the brim of the pelvis, with the danger of infecting the pelvic peritoneum and viscera in case of inflammation.

These are the principal positions of the appendix, but when the mesentery of the cecum is abnormally long and lax it may be found in almost any part of the abdomen.

Its length is also variable. It averages from 3 to 4 inches, but may be a mere stump, or as long as 9 or even 10 inches.

In *external appearance* the normal appendix is of a light pink color, and soft and velvety to the touch. Any hardness or rigidity is an indication of inflammation either past or present. Concretions or foreign bodies may easily be felt from the outside. The subperitoneal vessels can hardly be distinguished by the naked eye. It must be clearly remembered, however, that an appendix may appear normal to the naked eye, both in external appearance and even when cut into, and may yet be the seat of active inflammation. Lockwood, in his memoir on the appendix, cites several cases which bear this out very forcibly.

On *section* the lumen is seen to be Y-shaped, and is surrounded by the mucosa which is about 1 mm. in diameter. Separated from the mucosa by the somewhat open submucosa is the muscular coat, consisting of an inner circular and an outer longitudinal layer. The peritoneal coat can hardly be seen by the naked eye, and under it is the equally thin subserous layer.

The *mucous membrane* consists of a single layer of columnar epithelium, numerous tubular glands lined by similar cells, and masses of lymphoid tissue. The surface epithelium constitutes the most

important barrier against bacterial invasion. When it is broken down the bacteria in the lumen have ready access to the wall of the appendix.

The lymphoid tissue is arranged partly as a fine adenoid reticulum surrounding the bases of the glands, partly as definite follicles which are situated at the junction of the mucosa and submucosa. The follicles vary in number, but five or six may usually be counted in a transverse section through the middle of the appendix. Lockwood estimates that an appendix of ordinary length contains from 150 to 200 of these follicles. In the middle of the follicle is the "germinal center," pale in color, and containing proliferating cells which may

Fig. 107.—Appendix showing hiatus muscularis.

show mitotic figures. The outer part consists of a dense mass of darker cells.

It is probable that the abundant lymphoid tissue constitutes a defense against bacterial invasion. This tissue is most abundant during adolescence, and begins to atrophy about the thirtieth and sometimes as early as the twentieth year. These facts may have some bearing on the pathology of the organ.

The *submucosa* consists of delicate connective tissue, well supplied with blood vessels and lymphatics. It varies greatly in thickness as the result of disease. In acute inflammation it becomes swollen, edematous, and crowded with inflammatory cells. As the result of

repeated attacks it becomes converted into dense fibrous tissue. It is separated from the mucosa by the muscularis mucosæ, but this band is not nearly so well developed as in the rest of the intestine, and may be completely absent opposite the lymphoid follicles.

The submucosa becomes continuous with the subperitoneal tissue through certain gaps in the muscular coat. Such a gap is called a hiatus muscularis, and serves for the transmission of the blood vessels and lymphatics passing from the peritoneum to the mucous membrane. These gaps are situated chiefly along the line of attachment of the meso-appendix. Their great pathological significance is at once evident when it is recalled that infection starts in the mucous and submucous coats, and may thus pass through these gaps and give rise to peritoneal infection.

Anyone who examines a large number of appendices will be struck by the presence of fat in the submucous coat. This fat is sometimes so abundant that it is easy to recognize it by the naked eye in cross sections of the organ. I have seen cases in which the entire submucosa appeared to be converted into adipose tissue. This fat gains access to the submucosa along the line of the blood vessels which pass through the hiatus muscularis. Doubtless a similar appearance might be found in other portions of the bowel along the line of entry of the blood vessels.

The *muscular coat* consists of an inner circular layer about one millimeter in thickness, and an outer longitudinal layer of about half that diameter. When the appendix is distended by disease the circular coat tends to become compressed, but longitudinal fibers are separated from one another, so that the former affords a more efficient barrier than the latter.

Physiology.—Whether or not the appendix subserves a special function has not been finally determined. It appears most probable that it is merely a vestigeal organ. In herbivorous animals the food is bulky and contains a relatively small amount of nutriment, so that the cecum is complicated and frequently pouched. In carnivora, on the other hand, where the food is concentrated and rapidly digested the cecum is simple and even rudimentary. In animals living on a mixed diet, such as many rodents, apes, and man, part of the cecum apparently becomes atrophic, and is represented by the vermiform appendix. Many special functions have been ascribed to the appendix, but until one of these can be definitely demonstrated by the experimental physiologist it is useless to indulge in philosophical speculations.

Bacteriology.—The normal flora of the lower bowel is a varied one, and a routine bacteriological examination of the contents of the appendix will accordingly reveal many varieties of bacteria. Of these the bacillus coli is by far the commonest, but the streptococcus pyogenes, bacillus pyocyaneus, bacillus proteus vulgaris, and even anerobic organisms such as the bacillus aërogenes capsulatus, may occur, and may give rise to inflammation.

B. coli is the principal organism found in acute appendicitis, but it is by no means certain that it is always the primary invader, for other more delicate bacteria such as the streptococcus may be present which will be overgrown by B. coli unless special plate methods of investigation are used.

It is highly probable that many of the severe and virulent infections associated with a rapidly spreading peritonitis are due to the streptococcus, and the presence of this organism is always of bad prognostic omen.

In B. coli infections the type of the disease is milder, the inflammation is more localized, and there is a tendency to the formation of local abscesses, the pus of which has a characteristic fecal odor.

APPENDICITIS

In his exhaustive monograph on the subject Kelly remarks that "the vermiform appendix constitutes a microcosm, in which all the various diseases to which its component anatomical elements are liable in other parts of the body may occur." Of these by far the most frequent and important is acute inflammation.

Applying the principles already studied in the chapter on Inflammation we may say that the terminations open to inflammation of the appendix are (1) resolution with return to the normal, (2) tissue destruction with suppuration, ulceration, or gangrene, and (3) healing with the formation of cicatrices. It is seldom, however, that resolution is complete, leaving behind no ill effects. An appendix which has been the seat of a previous attack of inflammation may appear perfectly normal to the naked eye, but microscopic examination may show serious changes which strongly predispose to future inflammatory attacks.

We may therefore speak of (1) catarrhal appendicitis, (2) diffuse appendicitis with which may be associated ulceration or gangrene, and (3) appendicitis with stenosis. The last named is often called chronic appendicitis, but chronic inflammatory changes are not actually going on. The appendix is damaged and fibrosed, and is liable to recurring attacks of inflammation which vary in severity from the very mild to the very severe.

Etiology.—It is a curious fact that although appendicitis is such a very common disease the etiological factors still remain vague and indefinite. The frequency of the disease is only of recent date. Appendicitis was present, but was relatively rare, in highly civilized communities until the end of the nineteenth century. Since that time it has become very common in these countries. The rise began in England about 1895, and was pronounced between 1895 and 1905; since then it has been fairly stationary. It was in the cities and amongst the better-off classes that the rise was most marked; inmates of institutions on a plain diet are relatively immune.

The national distribution of the disease is very interesting. It is common in highly civilized countries such as Great Britain, the United

States, France, and Germany. In Denmark and Sweden it is lower. In Spain, Greece, Italy and the rural parts of Roumania it is very low. Lucas-Championnière found one case of appendicitis in 22,000 patients among Roumanian peasants, whilst in the cities of Roumania he found one case in every 22 patients. McCarrison states that during the 9 years that he practiced among the hill tribes of North-West India he never saw a case of appendicitis. In Asiatics, Africans, and Polynesians it is very rare, unless they take to European food; then it becomes common. In wild animals it is rare or unknown. In animals in captivity it is common, especially amongst the apes in Zoological Gardens.

Rendle Short points out that the link connecting these various facts may be found in the absence of cellulose and fiber from modern civilized food. It was between 1890 and 1905 that the chief change occurred owing partly to the great importation of food stuffs. In country districts and in institutions the older, simpler, and cheaper foods are still used. Natives who live on a diet containing an abundance of cellulose are immune from the disease, but whenever they turn to the diet of civilization they lose that immunity. Apes in captivity do not get the coarse foods to which they are accustomed in the wild state. Whether or not this explanation be sound, there can be little doubt that habits of life, and in particular modes of diet, are of great importance in predisposing towards appendicitis, and that meat-eating peoples are more liable to the disease than vegetarians.

The exciting case is equally elusive. Indeed, although foreign bodies such as oxyuris or concretions are occasionally found, and adhesions and kinks may obstruct the appendix, in the majority of cases it is impossible to say what has precipitated the attack.

Appendicitis may occur at any age, but it is rare in infancy and old age. It is commonest during the second and third decades. I have performed an autopsy, however, on a child two years of age with a gangrenous appendix, the clinical diagnosis being lobar pneumonia.

Acute Catarrhal Appendicitis.—Although this condition is frequently diagnosed clinically, it is by no means commonly found by the pathologist. In true catarrh the inflammation is confined to the mucous membrane, but in the appendix the natural tendency is for the infection to extend to the deeper structures, and to set up a diffuse inflammation.

The appendix is slightly swollen, and the subperitoneal vessels are dilated and tortuous. There is, however, no loss of the normal peritoneal sheen. The mucous membrane is swollen, edematous, and congested, and the surface is frequently covered with mucus.

Microscopically the surface epithelium is intact, but there is proliferation of the epithelial cells lining the glands. The stroma is congested and edematous, and contains considerable numbers of leucocytes. The germinal centers of the lymph follicles are unduly prominent, and contain many proliferating cells. The remaining coats of the appendix are normal.

Resolution may be complete, but residual changes are often left which predispose the appendix to subsequent diffuse attacks of more serious character.

Acute Diffuse Appendicitis.—The infection usually commences at the bottom of one of the crypts, and extends from the mucosa throughout the submucous coat, whence it may pass through the gaps in the muscular coat already alluded to, and thus affect the peritoneum.

The appearance of the appendix is very different from that seen in the catarrhal stage. The whole organ is enlarged, being elongated and thickened, it may be to several times the normal diameter. The color is bright or dark red, and there may be a purulent exudate on the peritoneal surface. Under the peritoneum there may be extravasations of blood, and perhaps yellowish spots indicating the formation of an abscess. The tip is often club-shaped, and the distension of that part may be marked. The mucosa is swollen and extremely congested. It is usually granular, and may be covered with warty processes.

Fig. 108.—Acute appendicitis with peritoneal exudate.

Erosions or ulcers of the mucosa are common. The ulcers are of varying depth, usually involving the mucous and submucous coats, but in some cases passing through the muscular coat as far as the peritoneum, where they may perforate. The lumen is filled with mucopurulent material.

Microscopically all the coats are congested, edematous, and infiltrated with inflammatory cells. These changes are most marked in the submucous and subserous coats. The epithelium of the surface and that lining the glands shows degenerative changes which may only be slight, but in many cases are profound. The glands are compressed owing to swelling of the interstitial tissue. Whole sections of the mucosa may be necrosed and cast off into the lumen,

these ulcers occurring especially at the points where the lymph follicles approach the surface. The surface of the ulcer is covered with fibrin and desquamated cells. If the process has gone on to suppuration small abscesses may be present in the wall. Threads of fibrin are frequently present, not merely on the peritoneal surface, but also in the inflammatory exudate in the substance of the wall. Hemorrhages may be scattered throughout the inner coat, often leaving permanent collections of pigment. The vessels are often thrombosed, a condition which may result, although fortunately only in exceptional cases, in the formation of septic emboli and pyemic abscesses in the liver.

The *course* of the disease depends largely on the peritoneal changes. Although some degree of peritonitis is always present, localizing adhe-

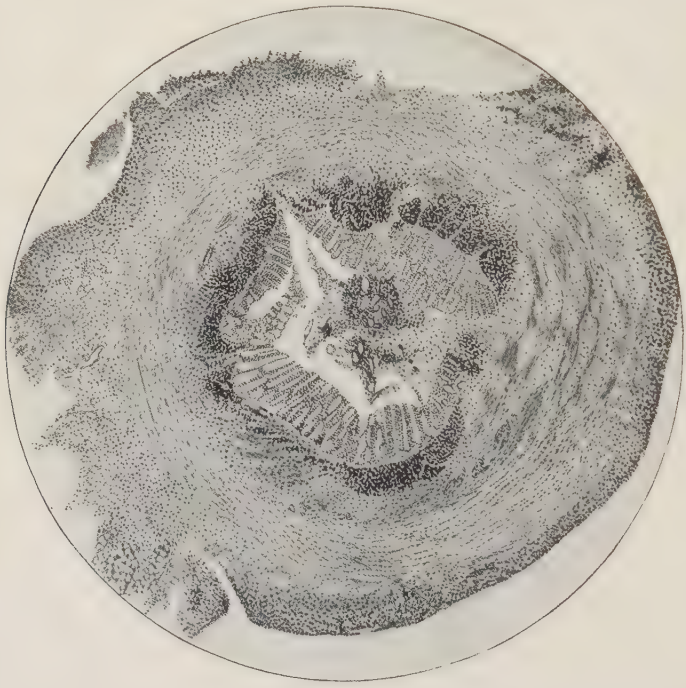

Fig. 109.—Acute diffuse appendicitis with peritonitis. All the coats are involved.

sions may prevent the spread of the inflammation, even when a local abscess has formed. On the other hand, and more especially in cases of streptococcal infection, the inflammation may extend rapidly from the submucous to the peritoneal coat, and set up a general spreading peritonitis even when the appendix does not appear to be very acutely inflamed. In these cases the symptoms of peritonitis mask those of the local appendicular lesion.

Gangrenous appendicitis is merely a further stage of the acute diffuse variety. There is death and putrefaction of the tissues of the appendix, either local or general, due in every case to interference

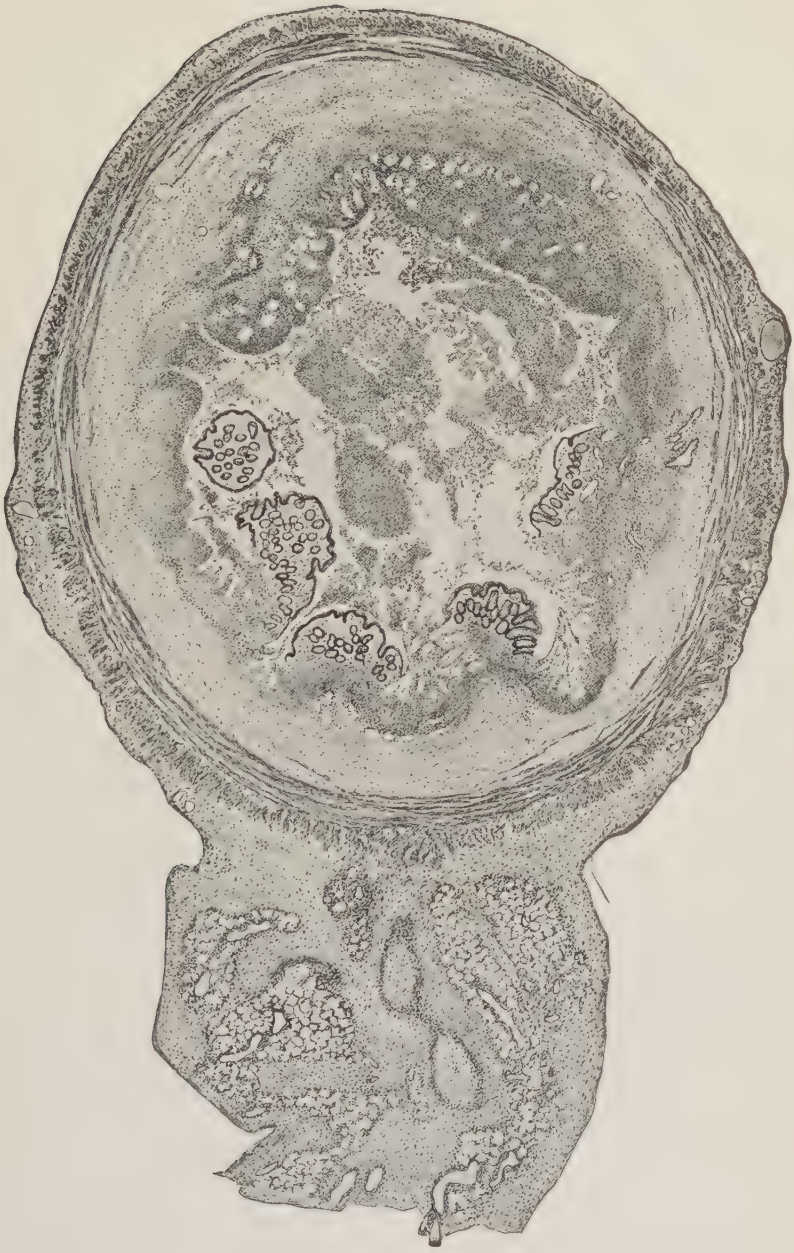

FIG. 110.—Acute diffuse appendicitis with great destruction of the mucous membrane. (MacCallum.)

with the blood supply. Such interference may be due to thrombosis of the vessels, to vascular obstruction from kinking or stricture of the appendix which is made acute by the sudden inflammatory swelling, or to pressure on the inflamed and swollen mucosa by a concretion.

If the main artery to the appendix be affected, or if there is obstruction and strangulation of the proximal end of the appendix, the whole organ may become gangrenous. More common is the development of a localized patch of gangrene, often at the tip, but there may be two or three such patches in both the proximal and distal parts. The affected area, which is of a green and later an almost black color, often corresponds to the position in the lumen of a hard concretion, which by pressure on the inflamed wall undoubtedly contributes to the production of the gangrene.

In cases of severe inflammation the meso-appendix shares in the general changes. It becomes thickened, edematous, congested, and infiltrated with inflammatory cells. Patches of mesenteric fat may be of so dark red a color as to resemble the appendix itself.

Perforation may occur at any stage of acute appendicitis. It may take place within the first 36 hours, or only late in the disease. It is due to necrosis of the coats of the appendix, of which the chief cause is the pressure of a concretion. Or it may be due to gradual erosion of the various layers. In rare cases it is due to the presence of a sharp foreign body such as a pin. The perforation may be pin-point in size, or may be a large yawning cavity with ragged edges. It is commonest at the tip, but may occur at any part. A small and unsuspected perforation may be found to be sealed over with a tag of omentum.

Acute Appendicular Obstruction.—Wilkie has emphasized the importance of distinguishing between two varieties of acute appendicular trouble, namely acute appendicitis and acute appendicular obstruction. The end result may be the same, but the method of production, the mode of onset, and the early clinical symptoms are different. In primary acute inflammation the pathological process commences essentially as an inflammation of the wall of the appendix. In primary acute obstruction, on the other hand, the essential lesion is the obstruction; the inflammation follows as a secondary consequence.

The peculiarity about the onset in acute appendicular obstruction is that at first the symptoms are purely local, and it is not until later that the general signs of inflammation manifest themselves. The important features distinguishing primary obstruction from primary inflammation are (1) the great severity of the pain, (2) the suddenness of its onset, and (3) the absence of disturbance of the pulse and temperature during the early stages of the illness. This absence of what are regarded as important indications of appendicular disease may be very misleading, but it must be realized that if acute inflammation of the appendix is a serious condition, acute obstruction is even more so, and calls for equally immediate operation.

Fig. 1.

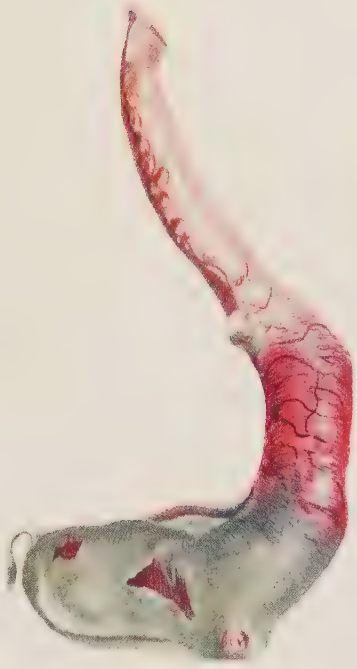

Fig. 2.

Fig. 1.—Appendix; carcinoma.
Fig. 2.—Acute appendicitis.

The predisposing causes of acute obstruction are (1) fibrous stenosis of the appendix, and (2) acute kinking of the appendix by a band or fold. The fibrous stenosis is due to some previous attack of inflammation, which often passes quite unrecognized; the narrowing of the lumen at the proximal end may be so extreme that only a pin-hole is left. A band or fold which causes abnormal fixation of the appendix at some point is a common cause of obstruction. Such a band may be an old inflammatory adhesion, but even more frequently it is a congenital fold which ties the middle of the appendix down towards the pelvis.

The *exciting cause* is a sudden access of fecal material to the partially obstructed appendix. This sudden access may be the result of straining or of some form of trauma, the latter being a not infrequent precursor of an attack of acute appendicular obstruction. A slight reaction occurs in the distal part of the appendix, and the associated swelling rapidly intensifies the obstruction or accentuates the kink. In some cases a concretion is found beyond the obstruction, and the irregular peristalsis of the appendix may drive it into the narrowed part, thus rendering the obstruction complete.

Wilkie has shown in a very interesting way the effect of varying conditions on an isolated loop of ileum the ends of which were closed. (1) When the loop was empty it became distended with mucus until a mucocele developed. (2) When the loop was moderately full of fecal material, the animal having been fed on a carbohydrate diet, an empyema of the loop gradually developed. (3) When the loop was full but the animal had been fed on a rich protein diet, the changes were much more acute, and the animal was dead within 24 hours. Complete gangrene may occur in 16 hours in a loop in which fecal matter has been locked up, even though there is no interference with the blood supply of the part.

The analogy to the conditions found in the human appendix is obvious. When an empty appendix becomes completely obstructed the result is a hydrops or mucocele of the appendix. When the obstructed appendix, contains some fecal material, probably not rich in protein, an empyema of the appendix gradually develops. Those common cases where distension and gangrene come on with startling rapidity correspond to the condition in the artificial appendix filled with feces after protein feeding.

This work on the relation of diet to the development of acute appendicular obstruction, which is borne out by the work of Heile on experimental appendicitis in the dog, throws some interesting light on such questions as the race incidence, the sex incidence, and the age incidence of acute appendicitis.

Reference has already been made to the prevalence of acute appendicitis in civilized communities and in cities as compared with uncivilized communities and rural districts. Speaking generally it may be said that in the former proteins are consumed, in the latter carbohydrates. Post-mortem statistics suggest that fibrosis and

scarring due to mild attacks of inflammation are common in all nations, but the urgent gangrenous type is confined to the meat-eating peoples. Acute appendicular disease is more than twice as common in the male as in the female. This may be due to the fact that the young adult male is more subject to strain and trauma, and that his diet is usually richer in protein than that of the female. Finally, the acute form is rare in the first years of life and in old age. In the former obstruction can not readily occur, whilst in the latter the lumen is often obliterated by fibrotic changes.

Chronic Appendicitis.—The clinical and pathological problems of acute appendicitis are simple compared with those of chronic appendicitis, the condition to which the clinician applies the name of the chronic appendix. The diagnosis of chronic appendicitis has become one of exceeding frequency, and it is one which it is often as difficult to refute as to confirm. Even when the appendix is in the hands of the pathologist he may find it difficult to say whether or not the specimen should be considered one of chronic inflammation.

The *symptoms* attributed to chronic inflammation of the appendix are legion, but the classical symptoms of the condition are vague abdominal pains, slight tenderness over McBurney's point, constipation as a rule, flatulence, "bilious attacks," "bilious headaches." The condition so aptly named by Moynihan appendix dyspepsia is characterized by pain coming on from half an hour to an hour after eating; there is no fixed interval of relief after a meal as in gastric ulcer, and the pain is described as coming on "at any time" after a meal; it is worse on exertion and after exercise.

Nothing is more difficult than to prove that the symptoms in all of these cases are due to lesions in the appendix. The pathological report depends largely on the personal views of the pathologist, and it has been said that to-day every appendix is condemned by some pathologist somewhere. Hospital statistics may also be quite misleading. The fact that the patient leaves the hospital with a diagnosis of "cured" means nothing. Visceroptosis is common in girls of from 12 to 24 years of age, and these patients often have tenderness on pressure in the right iliac region. Removal of the appendix affords relief for a few weeks, largely because the patient is kept in bed, but when she returns home the discomfort soon returns, and the operation is as unsatisfactory to the surgeon as to the patient.

The condition may be the sequel of one or more acute attacks. More often, however, it comes on insidiously. In such cases the symptoms are gradual in their onset, or there may be no symptoms, the condition being discovered accidently during operation for some other condition. Careful examination of many appendices removed in the first acute attack will reveal evidence of former inflammation, and it appears probable that acute inflammation occurs in an appendix already weakened by chronic inflammatory changes more often than in a healthy appendix, just as acute and subacute streptococcal endocarditis occurs in valves already weakened by rheumatism or syphilis.

Morbid Anatomy.—In discussing the morbid anatomy it must be realized that two different conditions are included in the term chronic appendicitis. (1) There may be a true chronic inflammation still in progress, or (2) the inflammation may have long since subsided, leaving a fibrosis which itself may be responsible for the symptoms owing to the production of stricture and of muscular inertia.

At first sight, then, it might appear that fibrosis, particularly of the submucous coat, is a sure indication of previous inflammation. When the appendix is buried in adhesions and shows marked kinking it is safe to say that the condition has been inflammatory; this is the picture seen in relapsing appendicitis, where there is a succession of definite acute attacks. Often, however, the appendix is quite free from adhesions, but shows the condition known as appendicitis obliterans, in which fibrosis of the wall leads to obliteration of the lumen, an obliteration which commences at the tip and gradually progresses towards the base. Such an appendix is commonly regarded as pathological, but it is difficult to see how it can be productive of symptoms unless there is at the same time a stricture at the proximal end.

On this matter there is much difference of opinion. Aschoff is very positive that obliteration from fibrosis is always due to a previous inflammation, whereas Ribbert, Zuckerkandl, and other authorities regard it as a more or less natural atrophic retrogressive process associated with the advance in years, and specially liable to occur in a vestigeal organ such as the appendix. In a series of 400 autopsies Ribbert found that 25 per cent of the appendices showed partial or complete occlusion of the lumen. The process of obliteration may commence at any point, but it generally begins at the tip and proceeds towards the base. Out of 300 specimens removed in the gynecological department of the Johns Hopkins Hospital, Kelly found that 45 presented some degree of obliteration. In a large series of appendices recently studied in the Winnipeg General Hospital many which were removed "en passant" in the course of another operation showed marked obliterative fibrosis unaccompanied by any symptoms. If the fibrosis is associated with stricture of the proximal end, symptoms due to appendicular obstruction may perhaps be expected, but when there is no stricture it is not easy to see why fibrosis in itself should give rise to symptoms unless, by interfering with the contraction of the muscular tube, it should prevent the normal emptying of the appendix. When, therefore, a fibrosed appendix is found in a case of chronic digestive disturbance it is hardly justifiable to assert with confidence that the condition has been merely one of "chronic appendix." The after history may tell a very different tale.

The most characteristic feature of chronic inflammation of the appendix is the thickening and rigidity of the organ. When the normal appendix is rolled between the fingers the walls are soft and the tube collapsable. The fibrosed appendix feels like a rigid incompressible tube. It may be longer than normal, but more often is shortened. It may be as thick as the little finger. The peritoneal vessels are dilated

and as tortuous as a corkscrew, and the color is redder than normal. Pale patches, particularly at the tip, indicate an obliterative process. There may or may not be adhesions: when present they are always an indication of previous inflammation. The meso-appendix is often thickened and shortened, as the result of which there may be kinking of the appendix.

On section the normal stellate appearance of the lumen is lost, and it remains circular and patulous. The lumen may be dilated owing to atrophy of the mucosa, or narrowed from the general thickening of the walls. Often the proximal part may be contracted, the distal part dilated. If the stenosis of the proximal part is complete, the remainder of the appendix may be distended with clear serous fluid (hydro-appendix or cystic appendix) or with pus (pyo-appendix or empyema of the appendix). The mucosa is usually thickened, but may be so thinned that it can hardly be seen. The normal smooth glistening appearance is lost, and the mucosa may be markedly granular, or smooth and glazed. It may be much congested, and minute petechial hemorrhages may be scattered over the surface. These are usually more marked in the distal part. Such an appearance of course indicates that the inflammation is still active, and is not represented merely by fibrosis. In many of our cases we have been surprised to find these petechial hemorrhages present in appendices which were removed incidentally from patients who presented no symptoms of appendicular disease. The occurrence of pigment granules is referred to in the microscopic description. The chief thickening is in the submucosa, which may constitute the greater part of the wall.

In appendicitis obliterans the gross picture is different. The withered appendix, which is very firm, is atrophic and shrunken, it may be, to the dimensions of a piece of stout string. The color is pale, uniformly so when the obliteration is complete, patchy when the process is partial. On section the appendix is seen to consist of two layers, an outer muscular layer, and an inner fibrous mass which includes what was once mucosa, submucosa, and lumen. The lumen may be completely obliterated, or it may be represented by a mere chink.

The microscopic picture varies considerably, with fibrosis as the one invariable feature. The principal change is usually found in the submucosa, which may be converted into a thick fibrous ring, or in the earlier stages may still show inflammatory granulation tissue. The subserous coat participates in the fibrosis of the submucosa, and sometimes it may be the site of the most marked changes, being thickened to an extraordinary degree. The muscular coat is more often atrophied than thickened, and the fibrosis is not usually very evident in this coat. The mucous membrane itself may show very little change; its stroma may be infiltrated with chronic inflammatory cells, especially lymphocytes and plasma cells; or the entire mucous membrane may be so replaced by fibrous tissue that the only hint of its former existence is the presence of a few islands of lymphoid tissue.

A very striking feature of many fibrosed appendices is the presence of fat in the submucosa. There is usually a little fat in this coat in the normal appendix; it is an extension of the mesenteric fat which passes in with the blood vessels through the hiatus muscularis. But in the fibrosed organ the amount may be enormous, and when the section is stained with Scharlach R. the picture is striking in the extreme. The fat, when abundant, can readily be recognized by the naked eye in cross sections from its light yellow color.

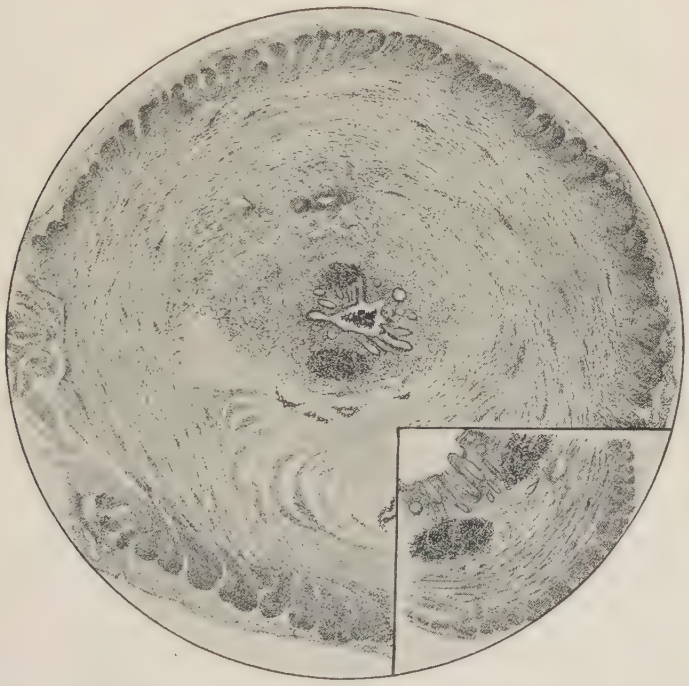

FIG. 111.—Fibrosis of appendix; inset shows normal thickness of the coats.

Granules of pigment may be found in the mucosa, probably the result of former hemorrhage. In one of our cases the mucosa appeared so brownly pigmented to the naked eye as to suggest deposits of melanin.

The microscopic changes so far described are due to former inflammatory attacks. But there may be evidence of inflammation of much more recent date in the shape of vascular engorgement and cellular collections. These changes are more readily recognized in the submucous and subserous coats. The mucosa is normally so cellular that it is usually very difficult to determine whether there is an infiltration with new inflammatory cells of the chronic type. In acute inflammation there is no such difficulty, for the inflammatory cells,

being polymorphonuclear in type, are readily distinguished from the normal cells of the part.

The usual cells found in the inflammatory collections are those which occur in chronic inflammation elsewhere, namely lymphocytes and plasma cells. They may be collected into little groups, or scattered more diffusely through the submucous and subserous coats. In a number of cases of chronic inflammation I have been surprised at remarkable collections of eosinophil cells. These have been observed in all the coats, but are perhaps most abundant in the mucosa. In some fields of the microscope these cells have been so numerous as to constitute over 50 per cent of all the cells present, and the picture recalls the appearance of the bronchial mucosa in asthma. The cells are of the polymorphonuclear type, whereas in asthma they are frequently mononuclears. In one case the serosa was infiltrated with polymorphonuclear eosinophils to such an extent as to suggest an acute inflammation. In this, as in other cases, however, there was no history of an acute attack at any time. The significance of these remarkable collections of eosinophils it is difficult, indeed impossible, to explain. An eosinophilia in the blood is found in a great variety of conditions, ranging from asthma and skin diseases to infection with animal parasites, but all connected by the common link of hypersensitiveness or anaphylaxis. A tissue eosinophilia, associated with narrowing of the smaller bronchi from inflammatory swelling of the mucosa, is one of the most striking histological features of bronchial asthma. What this has to do with the similar tissue eosinophilia found occasionally in the chronically inflamed appendix must be left an open question for the present.

Foreign Bodies.—In the diseased appendix it is common to find foreign bodies, which may simulate all kinds of familiar objects such as grape seeds, cherry stones, etc. It used to be commonly supposed that the stones of various fruits found frequent lodgment in the appendix, where they acted as the exciting cause of attacks of acute inflammation. It is now known that these are of the rarest occurrence, although it is true that many curious objects may find their way into the appendix. Pins, bristles, the stones of fruit, grains of corn, even small shot have been found in the appendix, but in many such cases the appendix may be quite normal.

Fecal concretions, however, are of very common occurrence. They vary greatly in consistence, being in some cases soft and putty-like, in others as hard as stone. Quite often they present a curiously laminated appearance which may cause them to be mistaken for gall stones. It is these concretions which were formerly mistaken for the stones of fruit.

The formation of a concretion is favored by stenosis of the proximal end of the tube, leading to a condition of stagnation within. The relation of concretions to the production of acute attacks has been much discussed. It is probable that they rarely act as a direct cause of an acute attack, but their continued presence may lead to chronic

changes which predispose the appendix to acute inflammation. Once an acute attack has commenced the pressure of the concretion on the inflamed and swollen mucosa may be responsible for necrotic changes in a way which has already been discussed.

RARE CONDITIONS

Tumors.—Innocent growths are so rare that they need only be mentioned.

Primary Carcinoma.—This is by no means so uncommon a condition as used to be imagined. Indeed MacCarty and McGrath at the Mayo Clinic found carcinoma in one out of every 225 appendices examined. The average age of their cases was thirty. In 90 per

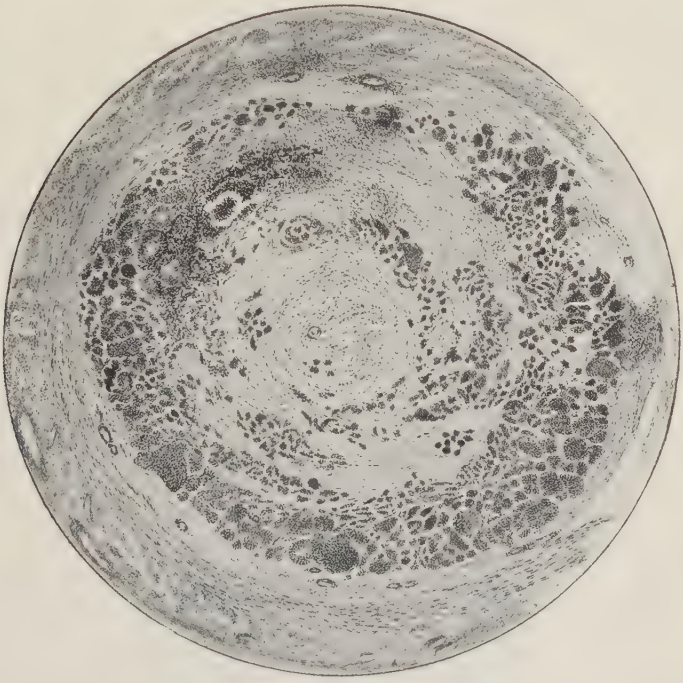

FIG. 112.—Carcinoma of appendix, showing masses of nevus-like cells. In addition to the tumor cells there is marked fibrosis.

cent the disease was situated near the tip of the appendix. Wilkie, however, has pointed out how a carcinoma at the proximal end may obstruct the appendix and lead to acute inflammation. He encountered three such cases in the course of 18 months.

The gross appearance is very characteristic. The appendix itself is thickened as the result of chronic inflammation. Until it is sectioned no other abnormality may be detected. Cross section reveals a yellow or yellowish-white ring which encircles the appendix and is

usually situated close to the tip. There is no evidence of infiltration, nor have metastases ever occurred in any recorded case.

Microscopically, the tumor consists of spheroidal cells arranged in very definite groups or masses, which occupy the mucous and submucous coats but show no tendency to infiltrate the peritoneal surface. This behavior, together with the invariable absence of metastases, is so unlike that of carcinoma that Aschoff suggests that the tumor is not a carcinoma at all, but rather a nevus-like growth occurring in a mucous membrane. The arrangement of the cells is certainly very like that seen in a nevus of the skin. In any case the general characters of the tumor are definitely benign, and it seldom causes symptoms and never the death of the patient.

Tuberculosis.—Tuberculosis of the appendix is usually secondary to tuberculosis of the cecum or of the Fallopian tube. In rare cases the disease is primary in the appendix. It may commence in the mucosa or submucosa, and gradually spread till the entire appendix is destroyed, and a large pericecal abscess forms which may discharge into the bowel or on to the skin surface. In other cases the first lesions are seen in the mesentery of the appendix.

Actinomycosis is usually secondary to disease of the cecum, but cases have been reported where the primary focus has been in the appendix.

Fig. 113.—Mucocele of the appendix.

In *typhoid fever* the lymphoid tissue of the appendix may show the infiltration with endothelial cells which is such a characteristic change in the ileum.

Mucocele of the Appendix.—As a result of obstruction of the proximal end of the appendix it occasionally happens that the appendix becomes dilated into a cyst. In a few cases complete or even partial obliteration of the lumen has not been present. These are cases in

which the contents are very thick and tenacious and the muscular coat may be deficient or completely absent. The cyst is usually small, but in rare cases it may attain an enormous size. One such cyst is described as being the size and shape of a very large banana (J. H. Kelly), and one is actually said to have been as large as a man's head (Neumann).

The contents of the cyst are usually somewhat thick and mucoid, and a true hydrops, in which the contents are watery, is a rare condition. The contents may give a reaction for mucin or pseudomucin.

These rare cysts of the appendix are of interest to the surgeon because they may be the starting point of a condition of *pseudomyxoma peritonei*, similar to that which occasionally complicates pseudomucinous cystadenomas of the ovary. As the result of rupture of the cyst the contents become implanted on the surface of the peritoneum, where they cause a proliferation with the formation of large masses like frog's spawn. The condition is probably due to implantation of the epithelial cells on the peritoneal surface, where they continue to produce their mucinous secretion, but other explanations have been suggested which are considered on page 393. The prognosis is unfavorable, but removal of the appendix may check the disease.

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CHAPTER XIX

THE RECTUM

The rectum is usually given separate consideration in textbooks of surgery. Although it is not our intention to give a full account of the surgical conditions affecting the rectum, which will be found in any of the text-books referred to, a few of the pathological problems may be considered in this place.

ULCERS OF THE RECTUM

Simple Ulceration.—Ulceration of the rectum frequently occurs without any discoverable cause. Numerous factors have therefore been suggested. Of these trauma is probably of considerable importance. Such trauma may be due to pressure of the fetal head during delivery, to the passage of hard scyballous masses, or, in rare instances, to the passage of a foreign body such as a fish bone. It is well to recognize, however, that many cases of ulceration of the rectum occur for which no possible cause can be assigned. If that be admitted it is more probable that the true key to the problem will one day be found than if the blame be attached to hypothetical scyballous masses or fish bones. The bacteria principally involved are the pyogenic cocci and B. coli.

No general description can be given of these ulcers. Although as a rule small and superficial, there may be extensive spread of the infection through the submucous coat, with wide destruction of the mucosa. Blood and pus are discharged in varying amounts, and there is a considerable amount of rectal irritation with frequent defecation.

Dysenteric Ulceration.—The rectum may suffer with the rest of the large bowel in dysentery, but the rectal lesions are of greater surgical interest than those occurring elsewhere, partly on account of the readiness with which they can be inspected, partly because of the tendency to stricture formation.

Ulceration may occur in the course of either amebic or bacillary dysentery. The ulcers are often so extensive that only tags or strips of mucous membrane may be left between them. The destruction of tissue is extreme, but perforation is not common. The causal bacteria or amebæ can be found in the stool. If healing occurs the great fibrosis will lead to equally great contraction, so that stricture formation may be a dangerous complication.

Tuberculous Ulceration.—Tuberculosis of the rectum is nearly always secondary to pulmonary tuberculosis. We cannot be certain

as to the route by which the tubercle bacillus reaches the rectum, but it is most probably by the blood stream. In a few cases infected sputum which has been swallowed may be the source of the infection. It is conceivable that tubercle bacilli swallowed in the food might set up the disease in the rectum.

Two main forms of rectal tuberculosis may be recognized: (1) that in which fistulous formation is the chief feature, and (2) that in which the chief feature is ulceration.

1. *Fistulous Form.*—The infection shows no tendency to spread over a wide surface, but burrows far into the deeper tissues. The ulcer, therefore, is small in extent, but an abscess slowly develops in the ischio-rectal fossa, which eventually discharges on the skin surface, with the formation of a fistula. The opening on the skin shows the characteristic undermined edges and bluish discoloration, the granulations are pale and prominent, the discharge is thin and watery and may contain tubercle bacilli.

2. *Ulcerative Form.*—This variety, which is distinctly less common than the preceeding, is characterized by the formation of extensive ulcers. Numerous tubercles are formed in the submucosa. These coalesce, large areas of caseation are formed, and the overlying mucosa becomes necrosed and cast off. The ulcers present the ragged, undercut edges characteristic of tuberculosis. So extensive may be the ulceration that the entire rectum may be involved. Tubercle bacilli are present in abundance in the discharge. Tuberculous ulceration is usually included in the list of conditions which may result in cicatricial stricture, but it is very doubtful if the lesions ever recover sufficiently for healing to occur.

Syphilitic Ulceration.—A very important if uncommon form of ulceration of the rectum is that due to syphilis—important because of the likehood that it may be mistaken for carcinoma. The condition is much more frequent in women than in men. For practical purposes we have to consider the tertiary stage, although a primary sore may occasionally be seen at the anal margin, and condylomata are common in the same region during the secondary stage.

As the result of gummatous formation in the submucosa there is extensive breaking down of the mucous membrane with widespread ulceration. The ulcer has the characteristic appearance of a syphilitic sore: hard and sharply defined edges, the base covered with a grey slough, the surrounding parts densely indurated. The ulceration may extend for some distance into the sigmoid. As the disease extends more deeply fistulæ may be formed communicating with the bladder, the vagina, or the skin.

There is another and rarer form of syphilis of the rectum, sometimes known as ano-rectal syphiloma, which corresponds with the diffuse syphilitic infiltration already described on page 115. In place of gummatous formation there is a diffuse formation of fibrous tissue in the submucosa, limited to the lower part of the rectum, as a result of which the rectum is converted into a rigid tube. There is little or

no ulceration. Subsequent cicatricial contration may cause marked stenosis.

Syphilis of the rectum should always be excluded before making a definite diagnosis of carcinoma.

RECTAL ABSCESSES

Abscess of the rectum and its neighborhood develops much more frequently in men than in women, and usually over the age of thirty. These abscesses may be divided according to their position into: (1) subcutaneous, (2) submucous, (3) ischio-rectal, and (4) pelvi-rectal.

Subcutaneous Abscess.—This originates as an infected sebaceous follicle or external hemorrhoid at the margin of the anus. The abscess usually discharges on the skin, but if it be not opened early it may burrow towards the rectum with the formation of a fistula.

Submucous Abscess.—When as a result of a tear in the mucosa infection gains an entrance, a submucous abscess will be formed. This may discharge on the mucous surface, or may burrow downwards to the skin, forming a blind fistula.

Ischio-rectal Abscess.—Infection may reach the loose cellular tissue of the ischio-rectal fossa as the result of an inflamed and thrombosed internal hemorrhoid, through an ulcer in the mucous membrane, or, quite frequently, through no apparent avenue.

The abscess which forms, and which is placed *below* the levator ani muscle, makes its way to the surface of the rectum and to the surface of the skin. It enters the rectum on its posterior aspect burrowing between the internal and external sphincters. A fistula is thus established between the interior of the rectum and the surface of the skin. Occasionally the abscess may extend round the posterior edges of the levatores ani and reach the ischio-rectal abscess on the other side, forming a "horse-shoe abscess."

Pelvi-rectal Abscess.—In a pelvi-rectal abscess the pus is situated *above* the levator ani muscle. Unlike the other abscesses in the neighborhood of the rectum the infection does not originate in the rectum but in some of the surrounding viscera such as the prostate, the neck of the bladder, or the pelvic bones. Not infrequently the pus makes its way through the levator ani and enters the ischio-rectal fossa.

HEMORRHOIDS

Hemorrhoids or piles is a condition in which the hemorrhoidal veins become varicose and hypertrophied. It is convenient to distinguish between two varieties: *internal piles*, involving the branches of the superior hemorrhoidal veins and covered by mucous membrane, and *external piles*, involving the inferior hemorrhoidal veins and covered by skin. Both forms are often present at the same time.

Etiology.—The etiological factors which may be responsible for piles are numerous and varied, but they all have this in common, that they induce a condition of congestion of the hemorrhoidal veins. The cause for this congestion may be central or local.

Of the *central causes* the two important conditions are a failing heart and cirrhosis of the liver with portal congestion. Of the *local causes* we may distinguish between causes within the rectum and those without the rectum. Examples of the former are any form of inflammation and chronic constipation. Constipation is the most important of all the causes of piles, partly because of the local injury to the mucosa produced by the hard scyballous masses, partly because of the pressure exerted, but perhaps chiefly from the tenesmus and straining which inevitably result in congestion and dilatation of the poorly supported hemorrhoidal veins. An important local cause for the appearance

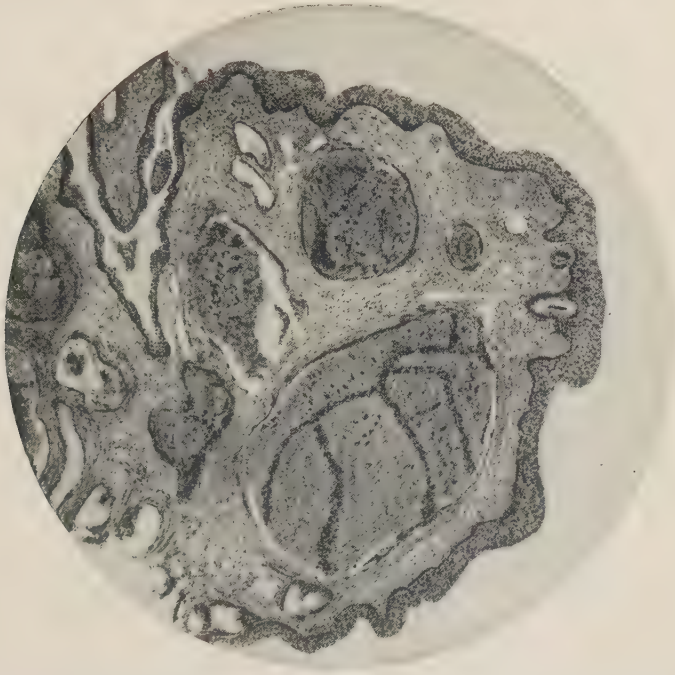

FIG. 114.—Hemorrhoids, showing the large blood spaces just under the columnar epithelium of the rectum and the stratified epithelium of the skin.

of piles, one which should never be out of mind, is carcinoma of the rectum. Amongst causes outside the rectum may be mentioned pressure from the uterus (retroversion of pregnancy), from the bladder (distension), and from the prostate (enlargement).

In addition to the direct or exciting cause of hemorrhoids it is often possible to trace a marked hereditary history in the cases. It has been suggested that as in varicose veins of the leg and in varicocele there appears to be some congenital weakness in the valves of the veins, so some such weakness should be looked for in hemorrhoids. It is much more probable, however, that it is the tendencies to constipation, etc. which are inherited.

Morbid Anatomy.—An internal pile, which may be taken as the common and characteristic variety, consists of a cluster of much dilated venules to which passes an artery, a terminal branch of the superior hemorrhoidal artery. This clump of vessels forms an elongated mass which lies in one of the columns of Morgagni, but later becomes more or less spherical. Secondary changes of considerable importance may take place. As a result of the chronic irritation a fibrosis occurs in the surrounding connective tissue which is responsible for much of the final thickening. Even more important is the occurrence of infection with the production of a periphlebitis and often phlebitis and thrombosis. The new tissue formed is therefore frequently infiltrated with chronic inflammatory cells, notably lymphocytes and plasma cells. The thrombosis may result in fibrosis with obliteration of the pile, or, if the thrombus is septic and becomes loosened, septic emboli may be set up in the liver. The patient may be subject to periodic attacks of phlebitis and periphlebitis, which are usually designated as "attacks of the piles." Such attacks tend to be self-curative, owing to the occurrence of thrombosis. Occasionally, as the result of straining on the part of the patient, the veins of an external pile will rupture, with effusion of blood into the surrounding tissue and the formation of a tense tender swelling under the skin. This may gradually become fibrosed, so as to form a firm nodule, or the clot may become infected and converted into a subcutaneous or perianal abscess.

The most important symptom of piles is hemorrhage. This, when continued over a long period of time, may lead to a profound degree of anemia, the cause of which may never be guessed, for the actual blood lost at any one time may be comparatively slight. The complexion becomes clay-colored, but the anemia is secondary in type, and should not be mistaken for the pernicious form of the disease.

INNOCENT TUMORS OF THE RECTUM

The innocent tumors of importance in the rectum are adenoma and papilloma.

Adenoma.—Perhaps the most interesting characteristic of adenoma of the rectum is its age incidence, for the majority of cases occur in childhood. The cases which occur in adult life differ from the cases of childhood in that they attain a much larger size, are usually sessile and often multiple, and not infrequently become malignant.

The adenoma of childhood is single and almost invariably pedunculated. The pedicle may grow to a great size owing to the constant traction exerted by the contraction of the bowel. In some cases it may become 4 or 5 inches long. Such a tumor is known as a rectal polypus. It is usually about the size of a raspberry, and with its dull red color and nodular surface it often resembles that fruit very closely. Hemorrhage is the principal symptom.

Microscopically the tumor consists of a wonderfully regular proliferation of the glands of the mucous membrane, the regularity form-

ing a marked contrast to the wild disorder seen in adenocarcinoma. There is, of course, no invasion of the muscularis mucosæ.

Papilloma.—This tumor, also called villous tumor of the rectum, although rare is of importance on account of its liability to become malignant. In many respects it resembles the villous papilloma of the bladder.

Occurring in adults, as a rule sessile or if pedunculated only slightly so, the mass is covered by long villous processes which wave gracefully to and fro when the specimen is placed in water. Each process is covered by one or several layers of cylindrical cells supported by a delicate stroma which is so vascular that hemorrhage occurs with

Fig. 115.—Diffuse papillomatous tumor of rectum.

great readiness. The extent of these tumors is sometimes remarkable. There is a specimen in the Pathological Museum of the University of Manitoba in which an area on the rectum the size of the palm of the hand is covered by red villous processes. The tendency towards invasion and malignancy is very strong.

Fibroma.—This tumor has been described as occurring in the rectum, but most if not all the examples have been merely inflammatory nodules. A thrombosed hemorrhoid converted into a hard mass of fibrous tissue has often been mistaken for a fibroma.

CARCINOMA OF THE RECTUM

The rectum is fifth in the list of primary seats of carcinoma, for over 5 per cent of all carcinomas occur there. Over 60 per cent of intestinal carcinomas are found in the rectum (Kaufmann).

A point of vital importance to the surgeon is that carcinoma of the rectum (and this is true also of the colon) is as a rule of comparatively slow growth and only of moderate malignancy; extension beyond the bowel wall and distant metastases do not occur early. If, therefore, the diagnosis can be made early, as it can if only the patient can be educated so as to consult the surgeon during the early stage, the disease is quite amenable to surgical treatment. Unfortunately the golden moment is usually allowed to slip past unnoticed.

As with cancer elsewhere the disease is one of middle and late life, but youth offers no certain protection. The first case which I encountered as a house physician was in a boy of seventeen, and cases

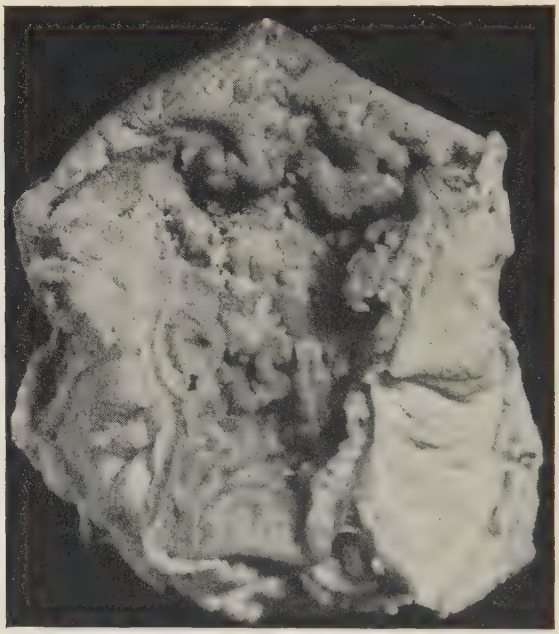

FIG. 116.—Carcinoma of rectum. The mucosa is ulcerated and the walls greatly thickened.

have been reported as early as the age of twelve. It usually proves fatal in from one and a half to two years, but some cases survive for a considerably longer time. Death is commonly due to some complication such as perforation of the bowel, peritonitis, or acute intestinal obstruction.

The tumor commences in the mucous membrane and gradually invades the deeper structures. As in the stomach and the intestine it may take a massive form and project into the lumen of the gut. Usually, however, it tends partially to encircle the bowel, producing a more or less annular stricture, and only at a later date does the overlying surface become ulcerated. The ulcer has the usual characteris-

tics of a malignant ulcer; the edges are raised and indurated, and the ulcer is crater-like. With ulceration the symptoms at once become aggravated. Of these the most noteworthy are a morning diarrhea which often alternates with constipation, hemorrhage, and toxic and cachectic symptoms which are due as much to the septic absorption as to the neoplastic process. The sudden development of internal piles and of a causeless sciatica are symptoms which should arouse suspicion.

Microscopically the picture is that of a characteristic adenocarcinoma or malignant adenoma. The transition between the normal and diseased mucosa is sudden and abrupt. The malignant cells not only replace the normal mucosa but penetrate the muscularis mucosæ, and irregular acini or solid masses are formed in the submucosa, throughout which coat the disease may spread with ease. The cells in time make their way through the muscular coat and appear on the peritoneal surface.

Methods of Spread.—There are three means by which carcinoma of the rectum may spread. These are (1) direct extension, (2) lymph spread, and (3) blood spread.

Direct Extension.—We have just seen that carcinoma commences as a nodule in the mucous coat. At this stage it is freely movable on the underlying muscular coat. As the submucous and later the muscular coats become involved this mobility gives place to fixation. Extension takes place in all directions, but more particularly transversely. It may be stated as a general rule that by the time the growth has encompassed half the circumference of the bowel it will no longer be movable. From a series of careful observations W. E. Miles came to the conclusion that the involvement of the circumference of the bowel is a comparatively slow process, and that it takes at least a year for three-quarters of the circumference to be invaded.

When the carcinoma has penetrated all the layers of the rectal wall its further advance is temporarily delayed by a large lymph space which separates the rectal wall from the fascia propria of the rectum. It is not until this space is crossed and the fascia propria invaded that fixation to the surrounding structures such as the sacrum, prostate, bladder, uterus, or vagina can occur. As this invasion seldom occurs before the growth has involved three-quarters of the circumference, that is to say before a year has elapsed from the appearance of the earliest symptoms, it is evident that if direct extension were the only means of spread the operative treatment would involve little more than excision of the affected part of the rectum. Unfortunately other methods of spread occur at a much earlier date and involve a much wider area.

Lymph Spread.—From the glands along the side of the rectum the lymphatics pass out in three directions, downwards, outwards, and upwards. The principal tissues involved in the *downward spread* are the skin around the anus, the external sphincter muscle, and the ischio-rectal fat. In the *lateral spread* the most important structures involved are the levatores ani muscles and the retrorectal glands;

at a later date the internal iliac glands, the base of the bladder and seminal vesicles, or the cervix uteri and posterior wall of the vagina may be implicated. The *upward spread* is the most important of all, and at an early date may involve many or all the glands in the pelvic mesocolon, and later the group of glands at the bifurcation of the left common iliac artery. Needless to say involvement of these glands cannot be detected by rectal examination.

Of these various structures the most vulnerable, those most liable to infection, are the levatores ani muscles, the retrorectal glands, the ischio-rectal fat, and the pelvic mesocolon. This will give some idea of the extent of the operation necessary for the extirpation of the disease.

Blood Spread.—Spread by the blood stream with metastases in the liver is, fortunately, a late manifestation of the disease. Occasionally, however, it occurs early. One of the largest livers I ever saw was the seat of carcinoma secondary to a growth in the rectum which was so small that it was nearly overlooked at the autopsy.

This is not the place to discuss the operative treatment of carcinoma of the rectum, but the recent symposium at a meeting of the British Medical Association clearly brings out the fact that there are few subjects on which surgical opinion differs more widely. In a series of 430 cases treated at the Mayo Clinic 33 per cent were alive 3 years after operation.

References for Further Study

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CHAPTER XX

THE GALL BLADDER AND LIVER

The Gall Bladder

Anatomy.—The normal gall bladder is 3 or 4 inches in length, with a capacity of about 1½ ounces. It is a thin-walled bluish sac, the inner surface of which has a velvety appearance, and is of a yellowish-green color. The bile in the gall bladder is darker and rather more viscous than that coming from the hepatic ducts, owing partly to the addition of mucus from the secreting epithelial cells lining the mucosa, partly to the concentration of bile which occurs within the organ.

The wall consists of a mucous membrane, a thick layer of plain muscle arranged somewhat irregularly and interspersed with fibrous tissue, and a peritoneal covering.

The usual anatomical description of the mucosa is that it is thrown into folds, but this conveys little to the mind until the gall bladder wall is viewed direct under that valuable instrument, the dissecting binocular microscope. When the fresh gall bladder, immersed in water, is observed by reflected light the picture is a remarkable and beautiful one. Tall graceful folds and membranes, gossamer-like in their delicacy, can be seen floating in the fluid like sea-weeds in a marine pool. The entire inner surface is divided by these membranes into a series of polygonal spaces, each of which resembles a little courtyard, surrounded by high though delicate walls. In microscopic sections the membranes, cut transversely, appear as villi. They are not true villi, but the term may be allowed because of its convenience. This striking picture at once suggests that the idea of the gall bladder as a mere reservoir is absolutely untenable. Such a highly specialized structure can be for one purpose only, namely absorption. In disease, as we shall see, the picture may undergo a complete change, and the delicate membranes become thickened, debased, and may finally disappear.

It is sometimes stated, even in well-known monographs dealing with the gall bladder, that the mucosa is studded with glands. This is not the case. The normal gall bladder shows no such glands. It is true, however, that in chronic cholecystitis the depressions between the villi become deepened and tortuous, until their connection with the surface may appear to be cut off, so that they may be mistaken for glands, an error made all the more possible by the occasional distension of the cells with mucin.

The efferent lymphatics of the gall bladder drain into the cystic gland, situated at the junction of the neck of the bladder and the

cystic duct. Thence the flow is into a number of lymph nodes along the common bile duct. Under normal circumstances the lymph flows to the receptaculum chyli; but when the passages are occluded by inflammation it may pass to the pancreatic plexus, and may thus convey infection from the gall bladder to the pancreas.

The gall bladder has a double nerve supply, partly cerebrospinal from the vagus, partly sympathetic from the ninth dorsal segment. The vagus is the motor and secretory nerve; it inhibits the sphincter. The sympathetic is the sensory nerve to the gall bladder, and the motor nerve to the sphincter. The nerve supply is of great importance in explaining the symptomatology of gall bladder disease, for the symptoms are usually referred to other organs such as the stomach. Inflammation of the gall bladder acts reflexly through the vagus and tends to cause hyperchlorhydria and regurgitation. In cases where the inflammation is more severe the sensory stimulus is greater, and a sympathetic reflex through the ninth thoracic segment results in pylorospasm.

The gall bladder must be regarded as merely a unit in a definite digestive complex made up of the liver, gall bladder, pancreas, stomach, and duodenum. These are all innervated by the sympathetic from the ninth thoracic segment, so that disease in one is apt to be reflected in some or all of the others, the stomach being the principal sufferer.

Physiology.—The function of the gall bladder is still a matter of debate. The fact that its removal in man does not appear to be attended by any untoward consequences must not be taken as an indication that it serves no useful purpose. A great difficulty which presents itself as a stumbling block in the way of any explanation of its function is the absence of the organ in a number of animals. Amongst those which possess no gall bladder may be mentioned the horse, the mule, the ass, the deer, the elephant, the rat, the pocket gopher, and the pigeon. Why the mouse should possess a gall bladder but not the rat, the striped gopher but not the pocket gopher, the hen but not the pigeon, is certainly difficult of explanation.

The gall bladder is not a mere reservoir for the bile, for its capacity is little more than an ounce, and it is probable that the daily production of bile amounts to nearly a liter. It has been suggested that one of its principal functions is to convert the continuous flow of bile from the liver into an intermittent flow into the duodenum. In support of this consideration may be cited the fact that the lower end of the bile duct is guarded by a sphincter (the muscle of Oddi) which is supposed to relax in response to the demands of digestion, so that a considerable volume of bile can flow into the duodenum at the moment when it is most needed.

This simple view entirely fails to explain certain facts which cannot be ignored. The recent experimental work of Rous and McMaster has shown that the gall bladder exerts a most remarkable concentrating effect upon the bile which passes through it. In some instances

the bile was concentrated as much as ten times. A simple reservoir does not concentrate the fluid which is contained within it. Moreover, the tall graceful, delicate folds, thin as gossamer, covered by a highly specialized columnar epithelium, and plentifully supplied with blood vessels, are surely designed for absorption rather then storage.

Great interest has been aroused recently by the idea that the contents of the gall bladder may be obtained through a tube passed into the duodenum accompanied by the application through the tube to the duodenal mucosa of a substance such as magnesium sulphate which is supposed to cause the sphincter of Oddi to relax and the musculature of the gall bladder to contract. Lyon, following a suggestion by Meltzer, has employed this method on an extensive scale both for purposes of diagnosis and treatment (so-called non-surgical biliary drainage), and is convinced that he can thus obtain first the bile from the bile duct (clear and light yellow), than the bile from the gall bladder (darker and more viscid), and finally the bile from the liver (lighter and more fluid).

If this be confirmed it is a most important advance, both diagnostic and therapeutic; it is almost as if one could look into the interior of the gall bladder and observe whether suppuration or calculus formation were going on there. Much has been written both for and against the idea. The most important, simple, and beautiful observations, however, are those of Auster and Crohn. These workers, using dogs anesthetized with chloretone, injected a solution of methylene blue into the gall bladder, opened the duodenum, irrigated the papilla with a 25 per cent solution of magnesium sulphate, and obtained a flow of bile, but not a trace of methylene blue even after a long interval. Compression of the gall bladder was at once accompanied by the appearance of methylene blue in the duodenum.

Such an observation appears to deal a serious blow to Lyon's idea that the result of the use of magnesium sulphate is an emptying of the gall bladder. The bile obtained by the duodenal tube must come from the hepatic ducts and the liver. In actual practice, however, the method may still prove to be a valuable one. Finkelstein, working in my laboratory on a large number of cases, found repeatedly that the bile obtained by the tube corresponded in its pathological condition with the bile subsequently obtained from the gall bladder. (One must guard against the fallacy that cloudiness of the bile from the duodenum indicates a pathological condition; it is often due merely to precipitation of the bile pigments and bile salts owing to the admixture of acid gastric juice.) If the one contained pus, so did the other. In a number of cases cholecystectomy was performed simply upon the duodenal tube findings, and in no single case did the latter prove to be wrong. The explanation may well be that infection of the bile passages and of the gall bladder necessarily go hand in hand, so that, although the bile contained by the tube may come from the ducts in the liver, the information obtained may well be applied to the gall bladder.

CHOLECYSTITIS

Cholecystitis is due to infection of the gall bladder with microorganisms. It may or may not be associated with cholelithiasis, but the presence of gall stones is not sufficient in itself to produce inflammation. It may aggravate an existing inflammation, but the stones (with one possible exception) and the inflammation are to be traced back to a common bacterial origin. The cholecystitis is the essential condition, the calculi are a mere incident. Moreover the symptoms of gall stones, apart from their passage through the ducts, are those of the accompanying cholecystitis. The pure cholesterin calculus, which is usually unaccompanied by cholecystitis, is therefore symptomless. The organisms most frequently found are streptococci, B. coli, and B. typhosus.

Reference has already been made to the intimate correlation of what MacCarty calls the gastro-duodeno-hepatico-pancreatic system with the gall bladder through the sympathetic fibers from the ninth thoracic segment. It is natural, therefore, that the pain and discomfort of cholecystitis should often be confused with those of gastric ulcer. There are, however, many points of difference; the pain of ulcer is relieved by food and alkalies, whereas in cholecystitis it is unaffected; in ulcer it comes on at certain times and during the night, in cholecystitis it is constant by day but absent at night; in ulcer it is aggravated by all foods, in cholecystitis only by some.

Avenues of Infection.—Infection may reach the gall bladder in four ways: (1) it may ascend from the duodenum, (2) it may descend from the liver, (3) it may be carried by the blood, and (4) it may spread from the liver to the gall bladder by way of the lymphatics.

1. *Ascending Infection from the Duodenum.*—Although this mode of infection is theoretically possible, in practice it is probably extremely rare. Microorganisms do not pass up the healthy bile duct. Moreover the healthy duodenum does not contain bacteria. Even in typhoid fever they do not choose this route.

2. *Descending Infection from the Liver.*—Large numbers of bacteria are carried by the portal blood stream to the liver, there to be destroyed. Should any escape, they may pass via the hepatic ducts and the cystic duct to the gall bladder. It is not only from the alimentary canal that bacteria may pass to the liver. A large portion of the portal blood comes from the spleen, an organ one of whose functions is supposed to be to filter out microorganisms and send them to the liver for destruction. The spleen may thus constitute a constant source of infection, and Moynihan refers to cases in which splenectomy was necessary to prevent the recurring formation of stones in the liver even after the gall bladder had been removed. The frequency of gall stones in hemolytic jaundice with splenic enlargement is well known; they occur in about 60 per cent of cases of this disease.

3. *Blood Infection.*—There can be no doubt that the gall bladder may be infected directly through the blood stream. Bacteria may be

present in the wall of the gall bladder although none may be found in the bile, just as it is often possible to demonstrate bacteria in the synovial membrane of a joint in cases of chronic synovitis when none can be detected in the synovial fluid. Rosenow has shown that in order to determine the existence of bacterial infection of the gall bladder, the wall of the bladder must be pounded up and added to the culture medium. Finkelstein has demonstrated the same absence of bacteria in the bile in many cases of chronic cholecystitis, strawberry gall bladder, and biliary calculi. These facts suggest a blood infection.

The most convincing evidence, however, is furnished by Rosenow's work on the elective localization of streptococci. This worker isolated organisms of a low grade of virulence, mostly green-producing streptococci, from the gall bladder wall, the bile, and the center of gall stones. These, when injected into the blood stream of animals, produced characteristic lesions of cholecystitis and choledochitis. The organisms had apparently acquired an elective affinity for these tissues. F. C. Mann's demonstration that the intravenous injection of such an irritant as Dakin's solution could produce acute hemorrhagic lesions of the gall bladder indicates how important an avenue of infection the blood stream may be.

It is probable that typhoid bacilli reach the gall bladder by the blood stream. When injected intravenously they have been found to produce embolic lesions in the stroma of the gall bladder mucosa. Some observers, however, following the same procedure, have recovered the bacilli in the bile descending from the liver.

It is probable that the method of blood infection accounts for those cases of acute cholecystitis which follow an attack of tonsillitis.

4. *Infection from the Liver via the Lymphatics.*—One of the most important of the recent advances in our knowledge of gall bladder disease lies in the recognition of the part which the liver may play in the production of cholecystitis. The work of E. A. Graham is of particular interest in this regard. In a series of 30 cases of cholecystitis he found inflammatory lesions in the liver in every instance. In 26 of these the liver was definitely enlarged.

The lymphatic connection between the liver and gall bladder is very free, so that it is evident that infection may readily spread from the one to the other. Although the infection from an acutely inflamed gall bladder may spread to the adjoining portion of liver, it is more probable that in most cases the spread is in the reverse direction. Bacteria may therefore reach the gall bladder from the liver via either the hepatic and cystic ducts or the lymphatics.

The lymphatics have also been credited with conveying infection from the gall bladder to the pancreas, thus explaining the occurrence of chronic pancreatitis as a complication of cholelithiasis, which Moynihan considers to occur in 12 per cent of cases. Although Deaver has championed this view it must still be regarded as *sub judice*. The question is discussed in the chapter on the pancreas.

Morbid Anatomy.—The condition of the gall bladder will naturally vary with the nature of the inflammation. The inflammation may be acute, usually suppurative in character, or it may be chronic. The chronic inflammation may or may not be preceded by an acute attack.

Cholecystitis is frequently associated with gall stones, but may occur without them. The longer the condition has lasted the more likely is it to be complicated by calculi. MacCarty found that in 365 cases of cholecystitis there were stones in 69 per cent of acute catarrhs, in 76 per cent of chronic catarrhs, and in 93 per cent of the advanced chronic inflammations.

Fig. 117.—Empyema of gall bladder. A dilated and thickened gall bladder which is now acutely inflamed and distended with pus.

Acute Cholecystitis.—Acute inflammation of the gall bladder may not pass beyond the catarrhal stage, or it may develop into an acute suppuration. In the former there is little to be seen by the naked eye beyond congestion of the organ. In the latter the gall bladder is evidently acutely inflamed. It may be distended with pus, particularly if the outlet be obstructed, the mucosa is of a bright red color, the peritoneal surface may be covered with an inflammatory exudate, and there may be adhesions to surrounding structures. The cystic lymphatic gland, situated close to the origin of the cystic duct, is

enlarged in both acute and chronic cholecystitis, and the glands along the common duct may also be enlarged.

The inflamed and distended gall bladder may rupture into the abdominal cavity or into a loop of bowel to which it may become adherent.

Microscopically the thickened and congested wall is infiltrated with polymorphonuclear leucocytes, areas of hemorrhage are frequent, and much of the surface epithelium may be desquamated.

When the acute inflammation subsides the infection may linger in the wall of the bladder, a condition of true chronic cholecystitis, and one predisposed to by the presence of calculi. Or it may clear up completely, but the new granulation tissue formed becomes converted into fibrous tissue, and the bladder wall is extensively scarred.

Chronic Cholecystitis.—Chronic cholecystitis may be the result of acute inflammation, or it may come on gradually and insidiously. The latter cases are apparently due to infection with some low grade irritant such as the streptococcus viridans.

The problem before the surgeon in determining whether a gall bladder is the seat of chronic inflammation is easy in the advanced cases, but sometimes extremely difficult in the early stage where there may be little or no change in the gross appearance. We have seen gall bladders removed on the strength of the duodenal tube findings, gall bladders which appeared to all intents and purposes normal, but which when opened showed the condition known as the strawberry gall bladder. Whether or not such gall bladders should be removed is another matter. One of the early changes is a loss of the normal bluish lustre; the surface becomes dimmed, whitish, and opaque, and the wall is sensibly thickened to the touch. The cystic gland is enlarged, and it may be the glands along the common duct.

Moynihan considers that even an early invasion of the submucosa by bacteria is often indicated by the development beneath the peritoneum of the gall bladder of a considerable deposit of fat. We have paid considerable attention to this point in our own work, and have arrived at the conclusion that whilst an accumulation of fat in the deeper layers of the wall is frequently observed in histological sections in chronic cholecystitis, the occurrence is not of sufficient frequency to make it a dependable criterion in diagnosis. The most remarkable collection of subserous fat which I have ever seen, which enveloped the entire gall bladder as in a thick blanket, was in an autopsy case in which the patient never had a single symptom of gall bladder disease, and in which the gall bladder itself was in every other respect perfectly normal.

When the gall bladder is opened the condition varies greatly with the stage of the disease. The mucosa may be edematous and swollen, deep red or purple in color. Under the dissecting microscope the change from beautifully thin to thick swollen villi is very striking. These become debased and eventually disappear. When gall stones are present the surface may become eroded, but it is remarkable how intact

the epithelium may be in the worst looking gall bladders. The stroma of the mucous membrane (called the submucosa by some writers) is plentifully infiltrated with inflammatory cells. These are mostly of the mononuclear wandering type, lymphocytes and plasma cells, with polymorphonuclears when the inflammation is more acute. In the later stages there may be an abundant formation of granulation tissue with numerous fibroblasts and other fixed connective tissue cells. Congestion may be marked, but hemorrhages as a rule are not common.

The depressions between the villi may be much deepened, and when the section happens to cut them off from the surface the glandular appearance may be very striking. It is no doubt such a picture as

Fig. 118.—Advanced stage of chronic cholecystitis. The reticulation of the wall is extreme. A large stone is impacted at the neck of the bladder. The tube at the side contains the clear watery contents.

this that has led to the statement that the mucosa of the normal gall bladder is studded with glands. The surface epithelium and that of the depressions may be distended with mucin, an indication of the amount of mucus which is added to the bile in the gall bladder during periods of inflammation.

The inflammation spreads to the muscular and serous coats. In both of these the characteristic lesions are dilated capillaries and focal collections of chronic inflammatory cells, although sometimes the infiltration is more diffuse. Edema is often a marked feature, and the subserous coat is much thickened. Large collections of fat may

frequently be observed in the subserous and muscular coats. As fibrosis continues the muscular and elastic tissue is entirely replaced by scar tissue, so that the gall bladder is converted into an inert bag. As a result of the scarring the inner surface becomes reticulated and honeycombed, presenting an interlacing network of fine bands, but eventually these also disappear and the lining becomes perfectly smooth.

The thickening of the wall may be extreme in degree, and the cavity is often much contracted. In one case which came under my notice a piece of drainage tube had been left in the gall bladder by mistake three years previously. The walls of the bladder were half an inch thick, and were so contracted upon the tube that no trace of lumen was left. A similar condition is often seen when the gall bladder has been full of calculi for a long time.

When the scar tissue involves the cystic duct the resulting obstruction gives rise to great dilatation of the gall bladder, the walls

Fig. 119.—Drainage tube left in gall bladder for three years. Extreme thickening of wall and contraction of cavity.

of which are very thin. The cavity is filled with clear, colorless, watery fluid which has been secreted by the remnants of the mucosa. Owing to the obstruction of the cystic duct the gall bladder contains no bile. The condition is known as *hydrops* of the gall bladder. If a pyogenic infection is superadded the bladder becomes filled with pus, an *empyema* of the gall bladder. The latter condition may of course occur in acute cholecystitis should the cystic duct become obstructed. The state of the gall bladder depends largely upon the balance between infection and obstruction. If infection be marked and obstruction slight or absent, the bladder will be small and thick-walled. If infection be slight but obstruction marked, the bladder will be dilated and thin-walled.

The Strawberry Gall Bladder.—One of the most interesting of the early results of chronic inflammation is the curious appearance first described by Moynihan, and to which the very appropriate name of

FIG. 120.—Strawberry gall bladder.

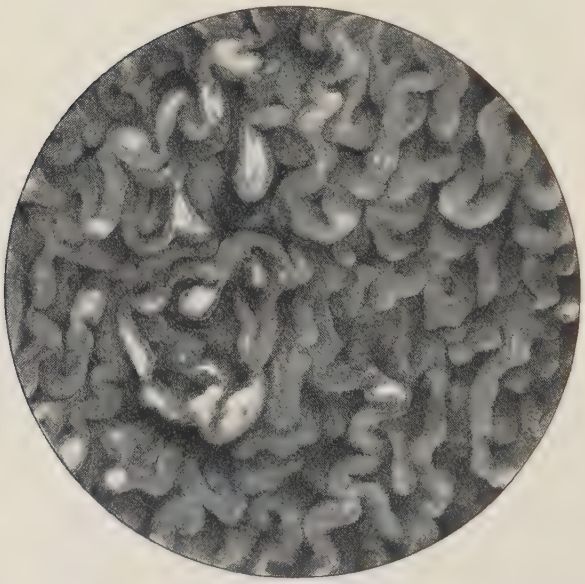

FIG. 121.—Mucous membrane of a strawberry gall bladder at an early stage. The patches of lipoid are whitish in color. Viewed through the binocular dissecting microscope.

strawberry gall bladder was given by MacCarty. The reddened mucosa is studded with tiny yellow specks, suggesting the seeds of a ripe strawberry. Sometimes the entire gall bladder is involved, at other times only one portion.

The condition is best studied under the binocular dissecting microscope. The graceful, fragile, gossamer folds of mucosa are completely altered in appearance, being loaded down by dense, yellow, opaque masses much as a delicate birch tree might be weighed down by a load of snow. Sometimes the yellow material is confined to the summit of the ridges, sometimes it can be traced down into the depth of the recesses. In the severe cases the distribution is widespread. In the milder cases it is more patchy, picking out a fold here and there, and giving the mucosa the appearance of a mountain ridge retaining only an occasional patch of the winter's snow. Before it is fixed in

FIG. 122.—Deposits of lipoid stained with osmic acid.

formalin the material can be lifted up in long strings by means of a needle as if it consisted of molasses.

The yellow material gives the usual reactions for fat. It is soluble in alcohol and chloroform, so that it cannot be seen in paraffin sections. It stains bright red with Scharlach R. and black with osmic acid. In these respects it behaves like neutral fat, which is an ester of glycerine, and which is sometimes found in large amount in the subserous tissue and in the deeper layers of the fibrous coat of the diseased gall bladder.

Although evidently of lipoid nature, it differs from ordinary fat in some important particulars. Of these the most noteworthy is its

behavior when viewed in frozen sections by polarized light under crosssed Nicol's prisms. Under these conditions neutral fat is quite invisible, but the lipoid of the strawberry gall bladder stands out in the most beautiful and brilliant manner, shining with a silvery radiance which is accentuated by the surrounding darkness. It is sometimes in the form of granular amorphous masses, frequently it appears as innumerable tiny needle-shaped crystals, and occasionally as bright Maltese crosses standing out against a black background.

The lipoid therefore displays the properties of an ester of cholesterin, and is of similar nature to the lipoid occurring in the adrenal cortex and the corpus luteum of the ovary. In this connection the

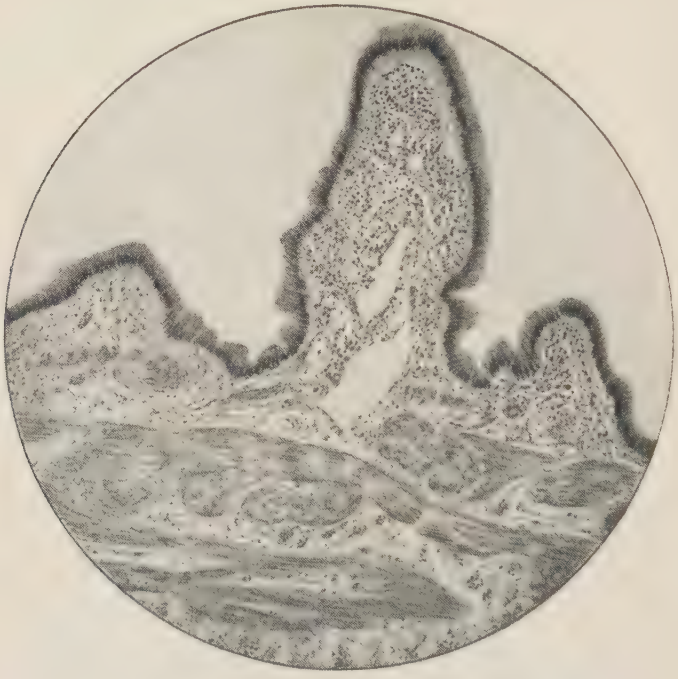

Fig. 123.—Lipoid at the base of the epithelial cells, and to a slight extent in the stroma.

well known relation between pregnancy and gall stones may be recalled to mind.

When cholesterin crystals are treated with concentrated sulphuric acid they turn a bright carmine red; with the ester the resulting color is a terra-cotta brown. We have succeeded in applying this test to frozen sections of the gall bladder, and the lipoid displays the same reddish brown color; this is a chemical test developed in the tissues.

The lipoid may be demonstrated without the use either of special staining methods or of the polarizing microscope. When a frozen section of a strawberry gall bladder is examined under an ordinary

Polypoid mass of cholesterol ready to separate. Early case of strawberry gall bladder. Stained with Scharlach R.

microscope with the diaphragm well closed, the lipoid is seen as dark, almost black, masses. Under the high power the acicular crystals can be made out with great distinctness.

Chemical estimations made in my laboratory show that the cholesterine content of the mucosa of the strawberry gall bladder is enormously in excess of that found in the normal organ. In one case it was sixty times the normal.

The distribution of the lipoid varies. In some cases it is confined to the surface epithelium, lying for the most part at the base of the cells. In other cases it is scattered throughout the stroma, both free and contained within wandering cells. In a few of our cases a very significant appearance was observed. The lipoid had collected in great

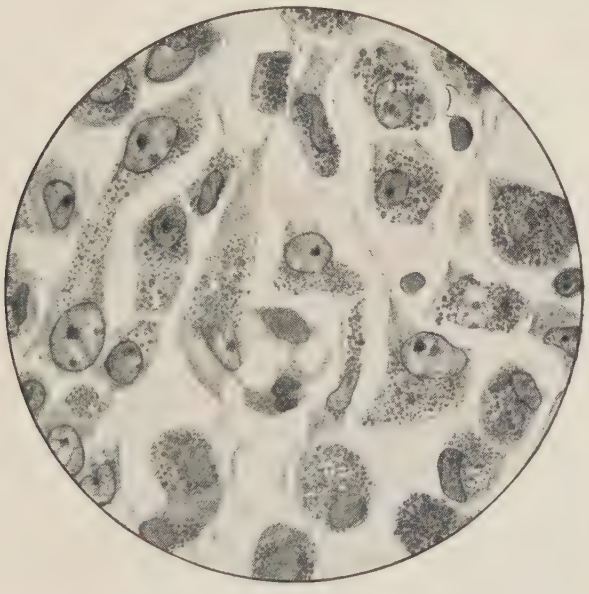

FIG. 124.—Inflammatory cells packed with lipoid granules.

masses in a villus, which now resembled a papillomatous process the stalk of which had become so attenuated that separation seemed inevitable. Should this occur we would have a foreign body composed of cholesterin and albuminous material lying in the cavity of the gall bladder, and forming an ideal nucleus for the formation of further deposits. The condition is well shown in Fig. 125.

It really appears that here we have a gall stone actually being formed in the gall bladder mucosa. How common a mode of formation of calculi this may be can only be determined by further investigation. Chauffard in a recent publication comes to a similar conclusion. He found that small biliary calculi may originate inside the villi as minute collections of cells surrounded by cholesterin; these are shed, grow, and ultimately become faceted.

We have found the lipoid in the gall bladder to be always associated with evidence of chronic inflammation. Whether this inflammation is the cause of the cholesterin deposits is a question which cannot yet be answered.

The Cholesterin Cycle.—The meaning of the cholesterin deposits in the gall bladder cannot be appreciated without a brief consideration of the rôle which cholesterin plays in the animal economy.

Cholesterin is a monatomic alcohol which, on account of its solubility in fat solvents, is regarded as lipoid. It is widely distributed in the animal and vegetable kingdoms, and is found in abundance in blood, bile, sebum, the white matter of the brain, the medullary sheath of nerves, the cortex of the adrenal, and the corpus luteum of the

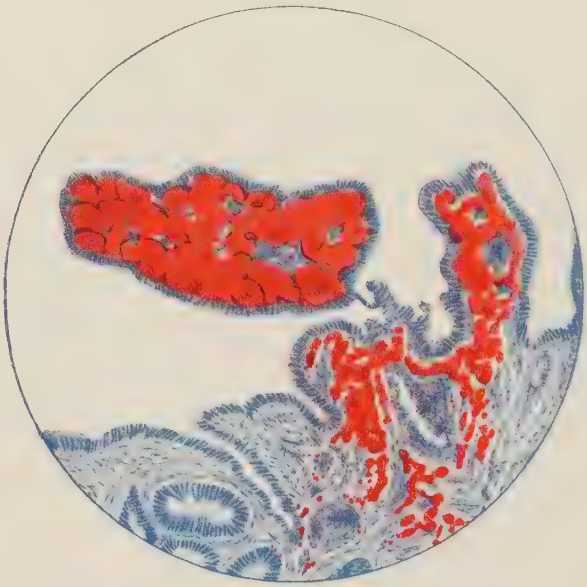

FIG. 125.—Masses of lipoid in the stroma. The surface epithelium is intact. Stained with Scharlach R.

ovary. Pathological deposits of cholesterin are found in arteriosclerotic blood vessels, in the white spots of albuminuric retinitis, in xanthoma, and in the kidney tubules in cases of nephrosis.

The blood cholesterin may be above normal. This rise may be temporary or more or less continuous. On this basis we may recognize two varieties of hypercholesterinemia: (1) obstructive, (2) constitutional. The former is due to obstruction of the common duct by a stone, and disappears when the obstruction is removed. As examples of the latter may be mentioned pregnancy, convalescence after typhoid fever, chronic nephritis, nephrosis, and diabetes. McAdam found a hypercholesterinemia in 60 per cent of Moynihan's cases of cholelithiasis, and it is more than possible that the remainder showed

an excess of blood cholesterin at one time or another. It is lowered in acute infections (with the notable exception of typhoid) and in tuberculosis.

The cholesterin in the feces is derived partly from the food, partly from the bile: that from the bile comes from cellular disintegration, chiefly, perhaps, the red cells which are broken down in the liver. Dorée and his associates found that the cholesterin in the feces of the dog amounted to only one-fifth of the total which might be expected from these sources. Moreover the cholesterin in the feces could be entirely accounted for by the cholesterin in the food. That in the bile had apparently been absorbed, excreted, and reabsorbed once more. It is this process which is designated by the term "the cholesterin cycle." It is known, of course, that other constituents of the bile—the bile salts and the bile pigments—are subject to a similar circulation with the object of preventing waste, a process which the French term the enterohepatic circulation.

The vital question presents itself: where does this absorption of cholesterin occur? My own work suggests that part of it at least occurs in the gall bladder. A consideration of the difference in concentration between liver bile and gall bladder bile supports the view that cholesterin is specially selected for absorption. The bile in the cystic duct is much more concentrated than the bile in the hepatic ducts, but the concentration does not affect all the solids alike. According to the figures given by Starling, sodium taurocholate is concentrated 16 times, sodium glycocholate 20 times, but cholesterin only 10 times. This suggests that some cholesterin is absorbed by the gall bladder mucosa in addition to the water.

If cholesterin is really absorbed by the gall bladder, it throws a considerable amount of light on the lipoid deposits in cholecystitis, and incidentally on the formation of calculi. Should some pathological factor inferfere with the process of absorption, precipitation of the cholesterin will occur in the mucosa and perhaps in the deeper coats. The most probable factor appears to be chronic infection.

GALL STONES

Gall stones may be formed in the gall bladder or in the bile passages. They may be single or multiple. The single are non-faceted, the multiple usually faceted. They are made up of cholesterin and calcium bilirubin, with frequently a framework of disintegrated cells. The following varieties may be distinguished.

1. *Pure Cholesterin Calculus.*—This stone is nearly always single, and is oval in shape, white in color, of a finely granular surface, and very light. On section it presents a characteristic radial crystalline structure. About 98 per cent of the stone is composed of cholesterin. There is usually no evidence of infection of the gall bladder. Indeed Aschoff declares that this type of stone is never associated with infection, but my own experience does not bear out so sweeping a statement.

The cholesterin stone is not accompanied by any symptoms unless it obstructs the cystic duct. In this it differs from ordinary gall stones which are always associated with cholecystitis, so that dyspeptic symptoms long precede symptoms of obstruction. Obstruction of the cystic duct by a cholesterin stone is accompanied by sudden terrible pain, and the cessation of the pain is equally sudden when the spasm of the duct relaxes and the stone becomes disengaged.

2. *The Mixed Calculus.*—This is the common type of stone. There may be a single, large, barrel-shaped stone, or several large faceted stones. On the other hand there may be large numbers of small faceted stones, differing so much in appearance from the large ones that one wonders if they can have the same origin. These stones are yellow or brown in color, of a smooth surface, and frequently possess a soft center and a hard outer shell. Occasionally they assume bizarre forms. For instance in our collection there is a set of calculi covered with knobs exactly like jack stones. As many as 7800 have been found in one gall bladder. The large and the small stones are not often associated together. On section the stone shows a series of concentric rings (compare with the pure cholesterin stone) some light, some dark, depending on the proportion of cholesterin to calcium bilirubin. These stones are always associated with some degree of cholecystitis.

3. *Calcium Bilirubin Calculi.*—These constitute what is known as biliary gravel, and take the form of large numbers of tiny, friable, blackish granules. They are composed almost entirely of the calcium salts of the bile pigments, with practically no cholesterin. This type of calculus is not infrequently found in congenital hemolytic jaundice, and it is of interest, in view of the absence of cholesterin in these calculi, to recall the idea that hemolytic jaundice is due to a lack of cholesterin in the envelope of the red blood cells. In one case of the disease which I studied the gall stones were of the usual size (not gravel), but contained no trace of cholesterin.

Gall stones may give rise to symptoms either during their passage along the cystic and common ducts or during their residence in the gall bladder. As regards biliary colic, it is true of the gall bladder as of the kidney that little stones like little dogs, makes the most noise. A large stone is more likely to remain in the gall bladder, more or less silent. Gall stones of the ordinary type are always associated with inflammation of the gall bladder. The cholecystitis is usually chronic in character, but not infrequently an acute attack may be superadded. Reference has already been made to the nervous mechanism by means of which the pain and discomfort in the gall bladder are referred to the stomach.

As a result of the chronic inflammation the wall of the gall bladder becomes greatly thickened, and its cavity may become so contracted that there is room for little else in it besides the calculi. This truth is expressed in the general rule known as *Courvoisier's law*, that in jaundice due to pressure on the common bile duct from without, as from cancer of the head of the pancreas, the gall bladder is distended, where-

Gall stones of various types cut and polished: 4, 7, 13, 14 and 17 show primary gall stones at first composed of almost pure cholesterine, later covered with pigment; 3, 5, 6 and 11 are faceted secondary stones; 9 and 19 show well the thin laminæ found under the faceted surfaces. (MacCallum.)

as in jaundice due to impaction of a stone in the common duct the gall bladder is usually contracted. A much dilated gall bladder, however, may contain stones. Thus a stone may be impacted in the cystic duct, so that the gall bladder becomes distended with mucus and yet at the same time it may contain numerous calculi.

The stone may be embedded in a deep pocket, through which perforation may occur. The danger of the stone perforating the wall of the gall bladder has already been referred to. Should the perforation occur into the transverse colon the stone is likely to be passed without trouble. When the perforation is into the small bowel the stone, if at all large, is apt to become impacted some distance above the ileo-

FIG. 126.—Biliary calculi entirely filling a much thickened gall bladder.

cecal valve. In one of our cases impaction at the lower end of the small intestine with symptoms of acute abdominal obstruction was caused by a stone the size of a pigeon's egg. It is difficult to understand how so large and hard an object could pass for such a long distance along the small bowel without causing such a degree of spasm as completely to stay its course. In most of the recorded cases, however, the obstruction has been at the same site.

Etiology.—The problem of gall stones is the problem of calculus formation in general, and cannot yet be said to be solved. There

are three factors which have to be considered. It does not follow that any one of them must be given pride of place in every case, for there may well be various conditions which will result in a precipitation of the solid constituents of the bile. The three factors are (1) bacterial infection, (2) stasis of the bile, and (3) a high cholesterin content of the bile.

1. *Infection.*—Of these three factors infection is probably by far the most important. Moynihan puts it in characteristically epigrammatic fashion: "every gall stone is a tombstone erected to the memory of the organisms dead within it; but sometimes the organisms are buried alive." The brilliance of the epigram, however, must not mislead us into applying it to every case of gall stones.

Experimental injection of virulent bacteria into the gall bladder does not give rise to the formation of calculi, but to an acute purulent inflammation which destroys the mucosa, a condition in which bile and bile-pigments are entirely absent. The introduction of sterile foreign bodies is also unaccompanied by the formation of stones. When, however, attenuated cultures are used, a mild inflammation is set up, and if this is accompanied by partial obstruction of the cystic duct owing to swelling of the mucosa, a calculus may result.

Infection is an important factor in determining the precipitation of substances usually held in solution. When a specimen of bile is inoculated *in vitro* with a culture of B. coli, precipitation of the cholesterin and of the bile pigments occurs. This is probably due to interference with the bile salts upon the presence of which the solubility both of the cholesterin and of the bile pigments depends.

Typhoid fever is a common cause of infection of the gall bladder, and in such cases the bacilli are often found in large clumps. Moynihan quotes a case in which the clumping suggested that a gigantic serum reaction had taken place in the gall bladder. Living typhoid bacilli may be found in the interior of the gall stones long after the original attack. Lewellys Barker mentions that living bacilli were found in a gall stone removed 35 years after an attack of typhoid fever.

2. *Stasis of the Bile.*—It is obvious that precipitation of the solids of the bile is much more likely to occur in conditions of stagnation than when there is a free outflow of bile. Such stagnation may be due to obstruction, a sedentary mode of life, muscular atony, interference with the innervation of the gall bladder, etc.

3. *The Cholesterin Content of the Bile.*—Two of the conditions most frequently associated with calculus formation, namely typhoid fever and pregnancy, are characterized by a great increase in the cholesterin content of the blood and therefore of the bile. Gall stones are much commoner in the female sex, (the proportion being 3 or 4 to 1), especially in stout women who have borne children, so that the old adage "fat, female, forty" in relation to gall stones contains much truth. But here again the danger in the past has been to overlook the importance of the gall bladder itself. As we have already seen the wall of the gall bladder may, under certain conditions, present an increase of the

Carcinoma of neck of gall bladder; early strawberry appearance in mucosa.

cholesterin content beside which any increase in the cholesterin in the bile fades into insignificance, and it is more than possible that in many cases the initial stage of calculus formation may take place in the gall bladder mucosa.

The factors which make for the formation of gall stones are apparently periodic rather than continuous in their mode of action. A collection of gall stones from one case are usually of the same size and type. They are all apparently born about the same time. Not infrequently different families may be recognized, but the various members of each family are all of the same birth.

The two factors most liable to periodic fluctuation are the cholesterin content and infection. The cholesterin content of the blood and of the bile will rise with each pregnancy, only to fall to normal in the intervals. Infection, again, is probably often periodic. The kidney in Bright's disease, the heart valves in endocarditis, may be the seat of recurring infections, after each of which the organ is left more and more damaged. So also with the gall bladder. The profoundly altered gall bladders which we often encounter are not as a rule the result of a single infection, but represent the cumulative effect of many such attacks.

CARCINOMA

The gall-bladder is peculiarly liable to malignant disease. A possible explanation of this lies in the relation of cancer to gall stones. In from 80 to 90 per cent of gall bladder carcinomas calculi are present. Indeed this relation affords one of the best examples of the causation of cancer by chronic inflammation. As might be expected, the disease is four or five times commoner in women than in men.

The disease may begin in any part of the gall bladder, but the parts most commonly affected are the fundus and the commencement of the cystic duct. The usual form is an adenocarcinoma, but in rare cases an epithelioma may be present, arising probably from a metaplasia of the columnar to squamous epithelium.

The same varieties of growth are found as have already been studied in the stomach and intestine, namely the papillomatous form and the diffuse infiltrating form. The latter is the more common, and gives rise to great thickening of the wall from a scirrhous growth. The liver is invaded early, and jaundice is one of the most constant features. In the papillomatous form the gall bladder is filled with a soft mass, which may occasionally become converted into a colloid cancer.

Carcinoma of the bile-ducts may affect the common duct, giving rise to complete obstruction, or more rarely it commences in a duct within the liver, where it constitutes the common form of primary carcinoma of the liver. It appears as a small, hard, white mass, which may be mistaken for a calculus.

THE LIVER

In many ways the liver is one of the most remarkable organs in the body. By far the largest of the glands, it exercises an all important

influence on the metabolism of proteins, carbohydrates and fats, so that it has been called the king of organs. In spite of the multiplicity of its functions it is extraordinarily simple in structure. Unlike the case of the kidney, each liver cell exactly resembles every other liver cell, so that the complexity must be within the individual cell rather than between the different cells.

There are, however, in addition to the bile ducts, two distinct types of actively functioning cell in the liver; these are the liver cells proper and the flattened endothelial cells, known as Kupffer's cells, which line the blood channels between the columns of liver cells. These endothelial cells are of such importance in the production of the various forms of jaundice that reference to them will not be out of place here.

The Reticulo-endothelial System.—The Kupffer cells form a part of what Aschoff calls the reticulo-endothelial system, which will be considered more fully in Chapter XXIX. This system comprises endothelial cells which are scattered throughout the body, but which attain special prominence in some organs after much the same manner as the lymphoid tissue. The cells are found particularly in the liver, spleen, bone marrow, and lymphatic glands; they constitute the interstitial cells of the testis, the reticular cells of the thymus, and the capillary lining of the adrenals. All of these cells are stained by intra-vitam methods of staining, whereas the ordinary capillary endothelium of the blood vessels remain unstained. The distribution of these cells is uneven not only throughout the human body, but in different animals. Thus in man they are mainly collected in the spleen but comparatively scanty in the liver, whereas in birds there are enormous numbers of Kupffer cells in the liver, but the spleen is quite small.

One of the chief functions of the reticulo-endothelial cells is concerned with the breaking down of hemoglobin. They are highly phagocytic, and in conditions of excessive blood destruction they are found to contain intact and broken down red cells. The presence of abundant hemosiderin can be shown by the Prussian blue reaction. It is this hemolytic activity of the reticulo-endothelial system which is of so much importance in the production of the condition known as hemolytic jaundice.

Three types of jaundice may be distinguished, namely obstructive jaundice, hemolytic jaundice, and toxic (including infective) jaundice. The common catarrhal jaundice is a combination of the first and third group. For the explanation as well as the detection of these we may look to the *van den Bergh reaction* for the presence of bilirubin in the blood serum, a full account of which is given in a very valuable paper by McNee.

The test, which is easily performed by adding a small quantity of serum to Ehrlich's diazo reagent, may give three types of reaction: (1) an immediate reaction, (2) a delayed reaction, and (3) a biphasic reaction which is a combination of both the immediate and the delayed types. The immediate reaction is obtained in obstructive jaundice (stone in the common duct, cancer of the head of the pancreas, etc.),

the delayed reaction occurs in the hemolytic variety of jaundice (hemolytic jaundice associated with splenomegaly, snake venom poisoning malaria, pernicious anemia, etc.), and the biphasic reaction is characteristic of toxic and infective jaundice.

McNee explains the mechanism of the jaudince in the following way. All bilirubin is formed by the breaking down of hemoglobin. In order to gain the bile duct it has to pass through the liver cell, but before reaching the liver cell it encounters the Kupffer cell. According to McNee it is in the latter that the bilirubin is actually formed, and not in the liver cell as is commonly supposed. The molecular constitution of the bilirubin is probably altered in its passage through the liver cell, and it is this altered bilirubin which gives the immediate reaction, the unaltered bilirubin giving the delayed reaction.

In obstructive jaundice the altered bilirubin is unable to escape, is reabsorbed into the blood, and the serum gives the immediate reaction. In *hemolytic jaundice* more bilirubin is produced than can be absorbed by the liver cells; the excess remains in the blood and gives the delayed reaction, whilst the altered bilirubin passes into the bile ducts and escapes into the duodenum. In toxic and infective jaundice it has long been recognized that there is a cholangitis of the finer bile-ducts which is probably partly responsible for the jaundice. But the liver cells are also involved, a phase of the subject emphasized particularly by the French. The cells are sick, this sickness ranging from cloudy swelling, as in pneumonia, to profound destruction, as in acute yellow atrophy. Some of the bile pigment may pass through still functioning liver cells and be reabsorbed owing to the obstruction to the bile ducts, whilst the rest is unable to pass through the damaged liver cells and remains in the blood. The result is a biphasic reaction.

Further light may be thrown upon the functioning power of the liver by some of the numerous tests recently introduced. Of these two of the most useful are the phenoltetrachlorphthalein test and the levulose tolerance test. The former is a test of the excretory power of the liver. *Phenoltetrachlorphthalein* is a dye which, when injected into the circulation, is excreted almost entirely in the bile. The amount which appears in the bile may be estimated by means of the duodenal tube, or, still better, the rate at which it disappears from the blood may be observed. If the liver is healthy the dye should completely disappear from the blood in the course of one hour.

The *levulose test* depends on the fact that levulose is the only sugar which when taken by the mouth does not produce a rise in the blood sugar. Glucose, although partly stored by the liver, also passes through into the blood where it can be readily estimated. Levulose is more readily stored by the healthy liver, and does not succeed in reaching the blood stream. If the liver is diseased, however, if the liver cells are sick, the sugar tolerance of the liver is lowered, and there is a rise in the blood sugar after the ingestion of 50 grams of levulose. This test gives striking results in toxic salvarsan hepatitis, and it

ought to prove very valuable for estimating the functional capacity before a surgical operation under prolonged general anesthesia.

Relation of the Liver to the Spleen.—The relation between these two organs is becoming of increasing interest to the surgeon. Both of them form an important part of the reticulo-endothelial system. The liver receives portal blood not only from the gastro-intestinal canal but also from the spleen. Indeed even in health 25 per cent of the blood in the portal vein comes from the spleen, and in disease, when the spleen may be enormously enlarged, this proportion must be infinitely

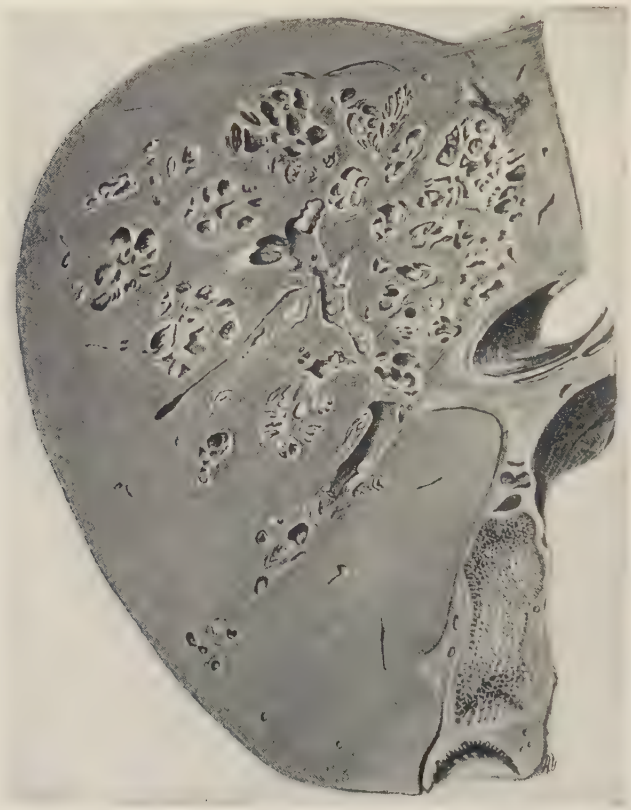

Fig. 127.—Multiple abscesses of the liver occurring in a general pyemia.

greater. The extra work thus thrown upon a weakened liver may complete its demoralization, or the spleen may fail to filter out bacteria and toxins from the blood and send them on for destruction by the liver, where they may produce profound disturbance. In either case it is evident that under certain conditions removal of the spleen may free the liver from overwork and from harmful influences, and may serve to arrest the development of such conditions as the various hepatic cirrhosis which in the past have been so far beyond the reach

of therapeutics. The relation of the liver to the spleen and the importance of both these organs in the production of the hemolytic jaundice associated with splenomegaly, so readily amenable to surgical treatment, is considered more fully on page 602.

The chief surgical conditions affecting the liver are abscess, tumors, and hydatid cyst.

ABSCESS OF THE LIVER

This may be due to infection (1) from the systemic circulation, (2) from the portal vein, and (3) from the bile-duct.

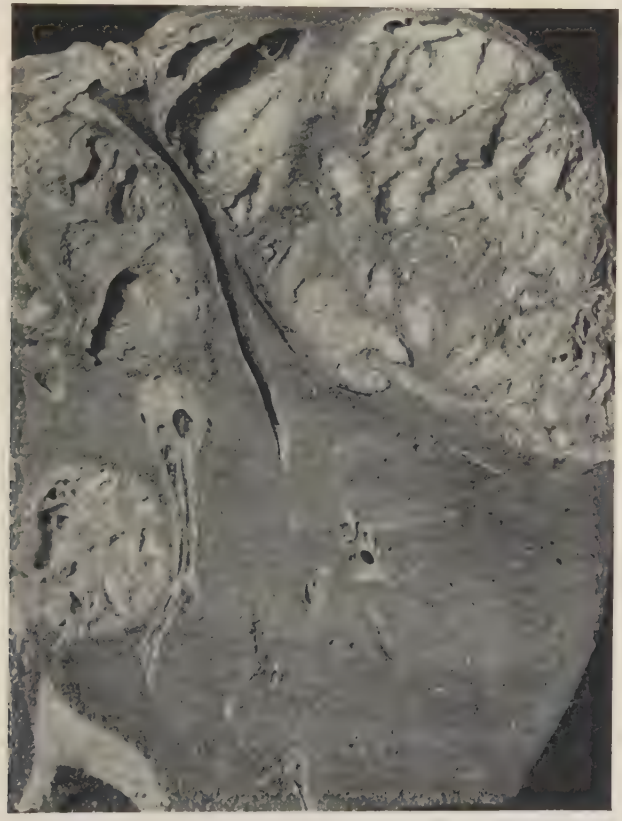

FIG. 128.—Abscess of liver. Portal infection from appendix.

In tropical countries the so-called *solitary abscess* complicating amebic dysentery is a common condition. Although the abscess may be single there are quite frequently several present. The common site is the upper part of the right lobe, producing upward displacement of the dome of the diaphragm on that side. The contents are viscid and chocolate colored, but usually inoffensive. The abscess may rupture into the peritoneum or into the lung. In some cases the pus becomes absorbed.

Small pyemic abscesses may be scattered throughout the liver in pyemia from any cause, but more especially in portal pyemia arising from such a condition as an appendicular abscess. It may seem remarkable that such pyemic complications are not more frequently seen after acute appendicitis, but the thrombosis which is in advance of the inflammation usually serves effectually to seal up the vessels.

Multiple *cholangitis abscesses* may be formed owing to calculus obstruction in the bile ducts in the liver associated with bacterial infection.

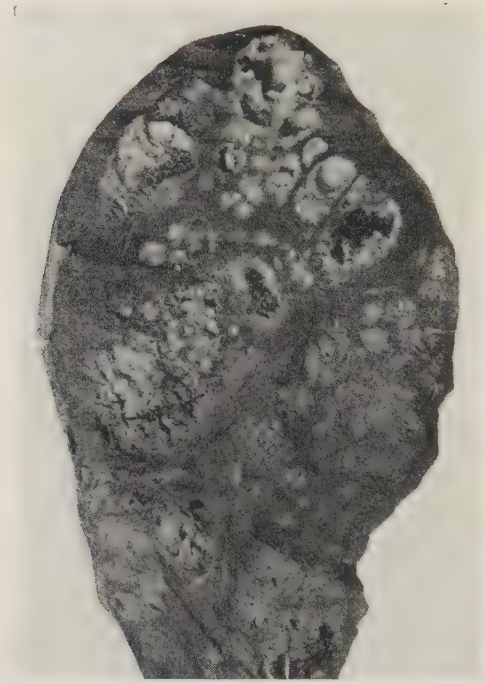

Fig. 129.—Cholangitic abscesses of the liver.

CARCINOMA OF THE LIVER

Carcinoma may be primary or secondary; the former is very rare, the latter comparatively common.

In the *secondary* form the tumors are metastases from growths elsewhere, usually from organs drained by the portal vein. Cancer of the breast not infrequently involves the liver. The nodules on the surface show a characteristic dipping-in or umbilication of the surface.

The *primary* forms may be of two varieties, the one arising from the epithelium of the bile ducts, the other from liver cells. The bile duct carcinoma is the commoner of the two. It is a columnar-celled

adenocarcinoma, usually multiple, many of the solid white masses attaining a very large size. Jaundice is a frequent accompaniment.

The liver-cell variety is a quite peculiar neoplasm. The entire liver is closely studded with nodules, and the intervening liver tissue is so profoundly scarred that I have known the error to be made of mistaking the condition for cirrhosis. The liver is considerably enlarged, and of a dark green color. Deep jaundice is a constant feature. The nodules are composed of broad strands of large cells, resembling liver cells, but with larger nuclei and more abundant cytoplasm, both

FIG. 130.—Secondary carcinoma of the liver.

of which stain deeply. The intervening tissue presents the same distorted appearance and dense fibrosis as is seen in ordinary cirrhosis. It is difficult to say which condition is the primary one, the malignancy or the cirrhosis. Are the carcinomatous nodules responsible for the irritation which results in cirrhosis, or does the cirrhosis cut off islands of cells which become carcinomatous? Another curious feature of the condition is that secondary growths outside the liver are unknown, and it has been suggested that the numerous nodules in the liver are

not metastases but are really all primary growths. Such a view, however, is difficult to accept even although no alternative can be suggested.

HYDATID CYSTS

These are common in countries where hydatid disease abounds, such as Iceland and Australia, rare elsewhere. The favorite site is the right lobe. The cyst may be single or multiple. It is surrounded by a fibrous capsule composed of compressed liver tissue. The true cyst wall consists of the usual two layers, an outer laminated membrane and an inner granular layer. The contents are clear opalescent non-albuminous fluid, scolices, and hooklets. The serum of the patient may give a precipitation reaction with hydatid fluid.

RARE CONDITIONS

Tuberculosis of the gall bladder is very rare. The symptoms may simulate those of gall stones. Tuberculosis of the liver often takes the form of large solitary masses, similar to those which not uncommonly occur in the brain.

Syphilis of the gall bladder is not of any importance. In the liver it may give rise to gummata, firm masses of varying size with caseous center, and leaving scars on healing which may produce great distortion of the organ. A diffuse inflammatory infiltration followed by characteristic scarring is a commoner manifestation of the disease.

Tumors Other than Carcinoma.—*Sarcoma* of the liver in the primary form is even rarer than carcinoma. Secondary sarcoma is also less common than secondary cancer. *Cavernous angioma* is occasionally found as a small red nodule on the surface. *Adenoma, cyst-adenoma,* and other innocent tumors of the liver are not of any surgical importance.

Cysts.—The commonest cyst is that due to hydatid disease. Simple cysts may occur, usually small, but sometimes as large as a cocoanut. Cystic disease of the kidney is in rare cases associated with a similar condition in the liver. In the only case which I have studied the cysts were no larger than a pea, although those in the kidney were larger than plums. In many of the recorded cases, however, the cysts attained a considerable size.

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CHAPTER XXI

THE PANCREAS

At the commencement of the gastro-intestinal tract there is a complex mechanism, made up of a number of organs, but acting physiologically and often pathologically as one whole, which MacCarty has called the gastro-duodeno-hepatico-pancreatic system. Not the least important member of this group is the pancreas, the most powerful of all the digestive glands, and yet one regarding disturbances of which we are still remarkably ignorant.

The pancreas not only produces digestive ferments which act upon the proteins, carbohydrates, and fats in the alimentary canal, but in addition it elaborates an internal secretion which exercises a most potent influence on carbohydrate metabolism, and probably also on the functional activity of the other ductless glands.

In view of these important activities it might be thought that disturbances of the pancreas would be readily recognized and diagnosed with accuracy. The reverse is the case. Acute disturbances, which are rare, closely simulate other abdominal catastrophies, and chronic disturbances are usually overlooked.

In chronic pancreatic disease substances will appear in the feces which are normally digested by the pancreatic juice. Fat in the feces renders them clay-colored or imparts an asbestos-like appearance. Other conditions than disease of the pancreas may however give fat in the stools. Chief among these is obstruction to the bile duct, since the bile plays an important part in the digestion of fat. Moreover, absorption of the fat may be interfered with owing to such a condition as tuberculosis of the bowel, giving rise to an abnormal amount of fat in the feces. These conditions must be borne in mind before arriving at too hasty a diagnosis of pancreatic disease.

Interference with digestion of proteins, as indicated by the presence of undigested muscle fibers in the feces, is frequently observed in disease of the pancreas.

The appearance of sugar in the urine is by no means a characteristic sign of pancreatic disease, even though the pancreas does exercise so important an influence on carbohydrate metabolism. Disease of the ordinary glandular tissue of the organ is not accompanied by diabetes. The relation of the islets of Langerhans to carbohydrate metabolism is now well recognized and it appears certain that in most cases of diabetes the islets are considerably sclerosed. In some, however, they appear to be unaffected.

The Cammidge reaction in the urine may be of some value if the services of a skilled chemist are available. Otherwise it is valueless.

Regarding this test Opie says: "The reaction has been obtained in a large proportion of instances in which pancreatic disease has been demonstrated or suspected. Nevertheless, the reaction may occur without pancreatic disease and is occasionally absent in association with lesion of the gland." It cannot be said that the test has established itself as a procedure of diagnostic value.

The chief pathological conditions affecting the pancreas are acute necrosis, chronic pancreatitis, cysts, and carcinoma.

ACUTE PANCREATIC NECROSIS

The term usually applied to this condition, acute hemorrhagic pancreatitis, is an excellent example of mistaken nomenclature. True, the condition is acute, but it may not be hemorrhagic, and it is certainly not a pancreatitis. Acute pancreatic necrosis is a descriptive term preferable in every way.

A great variety of names describing pathological conditions in the pancreas is found in the literature, such for instance as acute hemorrhagic pancreatitis, acute suppurative pancreatitis, pancreatic apoplexy, gangrenous pancreatitis, and chronic sclerosing pancreatitis. It is now possible, as Archibald in particular has emphasized, to regard all of these as differing manifestations of the same process. Such a conception in itself is a great advance in our knowledge of pancreatic disease.

Etiology.—If, then, these diverse conditions are at root the same pathologically, it is highly probable that they are all due to the same etiological agent. It is over this etiological agent and the route by which it reaches the pancreas that most of the controversy regarding pancreatitis has raged.

There are five possible routes by which an irritant may reach the pancreas: (1) by the blood stream, (2) by the lymph stream, (3) by direct contiguity from such lesions as ulcer of the stomach or duodenum, (4) by way of the bile passages, and (5) by regurgitation from the duodenum.

Although it is true that in rare cases metastatic involvement of the pancreas may occur via the blood stream, as in the acute swelling of the organ which may accompany mumps, it is unlikely that this is a factor of much practical importance.

The lymphatic theory, first suggested by Arnsperger, and championed latterly by J. B. Deaver, attributes the pancreatic lesion to the passage of infection from the gall bladder to the pancreas by way of the lymphatics. It is based purely on clinical observations, and has no support from experimental work. In cases of cholecystitis the surgeon often finds a chain of enlarged lymphatic glands in the course of the lymph paths between the two organs. The normal lymph flow, however, is from the pancreas to the gall bladder rather than in the reverse direction, and the lymph from the gall bladder could only reach the pancreas in the event of the normal paths toward the receptaculum

chyli being blocked as the result of inflammation. Deaver, however, declares that this is just what does occur, and that a pancreatic lymphangitis precedes the pancreatitis. According to him the usual sequence is cholecystitis, lymphangitis, lymphadenitis in the gastrohepatic omentum along the course of the cystic duct and the common duct, peripancreatic lymphadenitis, pancreatic lymphangitis, pancreatitis. In spite, however, of such distinguished support the matter must still be considered *sub judice*.

In exceptional cases it may be possible for the duodenal contents to be regurgitated into the pancreatic duct, as in those curious examples of acute pancreatitis in an accessory pancreas, where the duct opens into the duodenum at a distance from the opening of the common bile duct.

There can be little doubt that in the vast majority of instances the irritant passes from the common bile duct into the pancreatic duct, and thus reaches every part of the organ. Many substances, when injected experimentally into the pancreatic duct produce an acute pancreatic necrosis which is identical with the condition which occurs in man. Of these the most important are bile and duodenal contents.

The chief constituent of the bile in this respect has been shown by Flexner to be the bile salts, and particularly the taurocholate. Flexner also demonstrated that colloids, such as mucin, exerted a protective action, so that in conditions of chronic catarrh of the gall-bladder, in which the mucin content was increased, should the bile happen to enter the pancreatic duct the resulting reaction would be of a comparatively subacute or chronic character, with correspondingly mild clinical symptoms. If, on the other hand, the cystic duct be occluded, this protective mechanism is lost.

The experiments of Archibald and others have shown that the most acute and disastrous lesions are those produced by the injection of infected bile, particularly when the infecting organism is Bacillus coli.

Granted, then, that on both clinical and experimental grounds the most probable cause of acute pancreatic necrosis is the entrance of infected bile into the pancreatic duct, the question remains as to what is the mechanism by which the bile is forced into the pancreas instead of passing into the duodenum.

For long the views of Opie have held the field. The frequent association of pancreatitis with gall stones is well recognized. In a now celebrated case Opie found in an autopsy on a patient who had died of acute hemorrhagic pancreatitis that, not only was the gall bladder filled with stones, but a small stone was impacted exactly at the ampulla of Vater. As the common bile duct had joined the pancreatic duct a short distance from the common opening into the duodenum, the inevitable result was that the bile coming from the gall bladder was forced up along the pancreatic duct into the body of the pancreas. The view was soon adopted that all cases of acute pancreatic inflammation owed their origin to a mechanical obstruction of the diverticulum either by a gall stone or by a plug of inspissated mucus. In those cases

in which no stone could be found it was assumed that, after working its mischief, it had passed on into the duodenum.

Archibald, however, has pointed out that this theory is not a master key to the problem of the etiology of every case of pancreatitis. In a large number of cases no stones can be demonstrated either in the bile duct or in the gall bladder. There may, indeed, not even be any infection of the gall bladder. There must, then, be some other means by which the common opening into the duodenum may be temporarily closed. Such a means is provided by the muscular sphincter which exists at the outlet of the common duct, first described by Oddi in 1887, and called into recent prominence by the work of Meltzer and Lyon.

Archibald has shown in the most convincing manner that spasm of this muscle can be produced experimentally in cats, and that such spasm is followed by lesions in the pancreas which depend for their severity upon the nature of the entering bile. If the bile is heavily infected with bacteria, an acute hemorrhagic pancreatitis is the immediate result, and the animal is dead within two or three hours. Indeed in one experiment the cat died 20 minutes after the injection was complete with hemorrhagic necrosis of the entire pancreas. If the bile is less irritating the lesions will be correspondingly less severe, and in some instances a chronic sclerosing pancreatitis can actually be produced. The entrance of non-irritating bile into the pancreatic duct is probably of comparatively common occurrence, and may be either unattended by symptoms, or merely accompanied by mild abdominal disturbance of unrecognized origin.

Spasm of the muscle of Oddi may be induced experimentally by increasing the pressure within the gall bladder, as a result of which injected fluids may be traced into the finest ramifications of the pancreatic duct, or by the application of weak hydrochloric acid to the duodenal surface of the papilla. The latter observation is of interest in view of the frequency with which acute pancreatitis has been noted to follow the partaking of a heavy meal.

It is probable, of course, that in man a number of factors may be responsible for spasm of the sphincter. A heightened pressure within the bile passages, the passage of a biliary calculus, an excessive outpouring of hydrochloric acid into the duodenum, the reflex irritation produced by a duodenal ulcer, any of these may, it is easy to conceive, set up muscular spasm of sufficiently long duration to force the bile up against the low pressure encountered in the pancreatic duct.

The actual cause of the necrosis is probably the conversion of the inactive trypsinogen into active trypsin, an activation which, under normal circumstances, occurs in the duodenum owing to the interaction of the enterokinase with the trypsinogen. This conversion may occur within the substance of the pancreas owing to the entrance of duodenal contents or of bile. Normal bile produces little effect, but if rich in bile salts, and particularly when heavily infected with bacteria, the trypsinogen is converted into trypsin, and digestion of the pancreatic tissue immediately ensues.

Crushing injuries of the pancreas may result in the death of some of the pancreatic cells, and these undergoing autolysis liberate a substance which activates the trypsinogen, and the trypsin thus formed may lead to pancreatic necrosis.

The *cause of death* appears to be an overwhelming of the patient by the poisonous split-protein products formed as the result of partial digestion of the pancreatic tissue. The wholesale absorption of these intensely poisonous substances accounts for the extraordinary rapid termination of many of the cases. It is the same mechanism which has been shown by Whipple to be responsible for the intoxication in high intestinal obstruction.

An undue amount of space has perhaps been devoted to these etiological considerations, but it is evident that without a sound etiology rational treatment is impossible. Instead of directing a futile attack against the pancreas—for, after all, an acute necrosis cannot be drained—it appears more reasonable to relieve the pressure in the gall bladder, and, it may be, to prevent the recurrence of attacks of pancreatitis by interfering with the sphincter of Oddi.

Gross Appearance.—The naked-eye changes are usually striking and spectacular. It must be remembered, however, that acute necrosis may exist in a pancreas which is apparently normal. The varieties originally described by Fitz as hemorrhagic, gangrenous, and suppurative are merely subdivisions of the one process. The pancreas is usually enlarged, sometimes to two or three times the normal size, of varying consistence—hard in the milder forms, very soft and friable in the more severe types—and the surface may show opaque whitish areas of fat necrosis, extensive areas of hemorrhage, or it may be black and gangrenous. The changes may be confined to the head, or may involve the entire organ. In many cases there is no hemorrhage. In others the hemorrhage dominates the picture.

The result depends on the extent of the necrosis. If only small areas are involved they may be absorbed and replaced by fibrous tissue. Larger areas break down, become infected with bacteria, and give rise to abscess formation. The greater part of the pancreas may slough away.

A very characteristic feature is the presence of a sanguinous or sero-sanguinous exudate in the lesser sac of peritoneum. This exudate contains pancreatic ferments, and is as a rule sterile. It has been shown to exert a protective influence, so that it cannot be removed with impunity. Later, however, it may become infected and give rise to an acute peritonitis.

Fat Necrosis.—Perhaps the best known phenomenon of acute pancreatic necrosis is the occurrence of the peculiar white spots known as fat necrosis. These areas are of a dull, opaque, whitish appearance, contrasting strongly with the yellow glistening fat by which they are surrounded. They are most abundant in the vicinity of the pancreas, but may be scattered far and wide over the mesentery and the omentum. The subperitoneal fat of the abdominal wall may

be involved, and the change has even been found in the pericardium and the mediastinum.

That these areas are directly due to the action of the fat-splitting ferment of the pancreas has been proved by the discovery within them by Flexner of the pancreatic lipase. The neutral fat is broken down into glycerine and fatty acids, and the latter soon combine with calcium to form an insoluble soap. The areas tend to be absorbed in the course of a few weeks.

If the fat necrosis is due to the liberation of the pancreatic ferment it may be asked why the necrotic areas should be discrete and patchy.

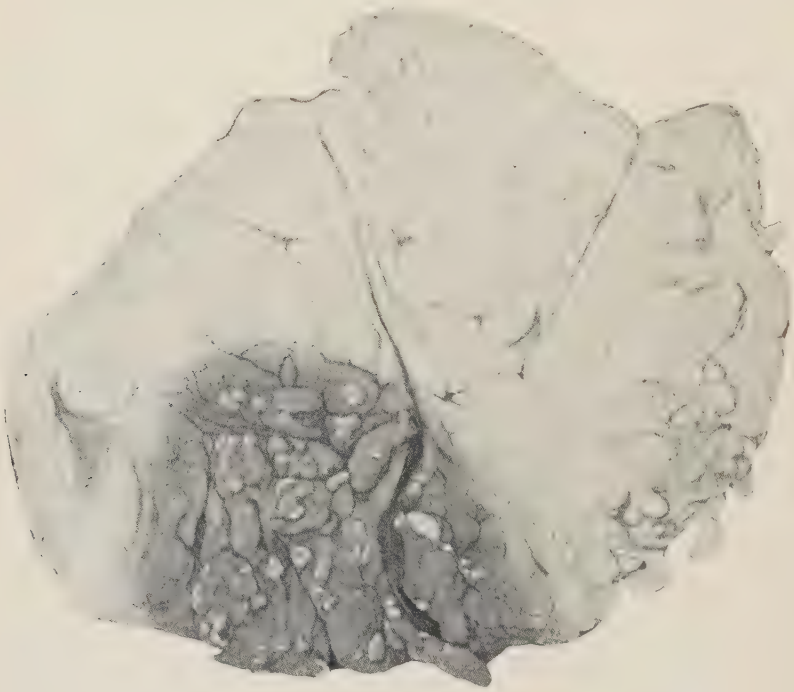

Fig. 131.—Pancreatic fat necrosis in the omentum. (MacCallum.)

The answer is that the digestive fluid cannot have flowed over the surface of the fat, otherwise the change would be a diffuse one. Moreover the epithelium covering the affected patches is quite intact. The lipase must have been carried by the lymph or possibly by the blood channels, picking out here and there an area for attack.

Fat necrosis always indicates a coexisting pancreatic necrosis, although in some cases the pancreas is to all appearances normal. In a recent autopsy on a case of carcinoma of the cervix uteri numerous areas of fat necrosis were found around the pancreas, although that organ was of the usual size and consistency. Microscopic examination, however, showed typical areas of pancreatic necrosis.

CHRONIC PANCREATITIS

Chronic pancreatitis is a diagnosis which is rather frequently made by certain surgeons at operation. It is seldom however, that a subsequent pathological examination confirms this surgical diagnosis, which is based on the fact that the head of the gland is found to be enlarged and hard. Few organs vary normally in size to a greater extent than the pancreas, and a gland which appeared much enlarged on the operating table may be of quite normal size at autopsy a few days later. Most of this swelling and firmness are due to an edema which may only be transitory, and is probably dependant on infection of the biliary passages. The condition is readily mistaken for carcinoma of the head of the pancreas, and a differential diagnosis may be difficult or impossible.

The term chronic pancreatitis should be limited to those cases in which there is a definite fibrosis of the organ. This fibrosis, as Opie has pointed out, may be of two main types interlobular and interacinar.

In *chronic interlobular pancreatitis* there is an increase of the fibrous tissue between the lobules, but with little penetration into the lobules and between the acini. There is marked atrophy of the acini and loss of the external secretion of the pancreas, with accompanying digestive disturbance. The islets of Langerhans are not involved, for they do not belong to the acinar system. There is, therefore, no glycosuria. The pancreas is hard, and the normal lobulation is rendered more marked.

It is probable that a variety of causes leading to retention of the pancreatic secretion in the ducts may give rise to this condition; such, for instance, are pancreatic calculi, a biliary calculus impacted at the ampulla of Vater, new growth or cicatrical stenosis from duodenal ulcer leading to narrowing of the opening, etc. Repeated entry of comparatively non-irritating bile into the pancreatic duct owing to spasm of the muscle of Oddi may well be a factor of great importance.

In *chronic interacinar pancreatitis* the new fibrous tissue penetrates between the acini and invades the islets of Langerhans. Glycosuria, therefore, is a prominent symptom. The lobulation of the gland is not increased.

Little can be said with confidence as to the cause. Arterio-sclerosis is usually mentioned, in an attempt to relate the condition to chronic interstitial nephritis. Warthin's demonstration that the pancreas is frequently attacked in a diffuse manner by the spirocheta pallida has brought syphilis to the front as an etiological factor of importance.

PANCREATIC CYSTS

Cysts of the pancreas, although far from common, are not so rare as used to be supposed. They may be divided into three groups: (1) cystadenomata, (2) retention cysts, and (3) pseudocysts. Of these the last are by far the most important.

Cystadenoma.—These are true tumors. The tumor is often multilocular, spaces are lined by high epithelium, and papillary processes may project from the walls.

Retention Cysts.—These are small cysts, the origin of which is somewhat uncertain. Ligature of the pancreatic duct is not accompanied by cyst formation, but it may be that intermittent or partial obstruction may result in dilatation of the duct, as in the case of the ureter. Chronic interstitial pancreatitis is often associated with the cyst formation, but it may well be a result rather than the cause of the condition.

Pseudocysts.—Most of what are called cysts of the pancreas are not cysts at all, but pseudocysts. They may attain a considerable size, and may be mistaken for echinococcus cysts, ovarian cysts, hydronephrosis, or a perinephritic abscess. They are not situated in the substance of the pancreas but in the immediate neighborhood, usually in the lesser sac of peritoneum which lies immediately in front of the pancreas. In this group may also be included the degenerative cysts which develop in superficial portions of the pancreas which have broken down as the result of acute pancreatic necrosis.

The chief causes of pseudocysts are a previous attack of acute necrosis and injury to the pancreas from trauma. As the result of a superficial lesion there is an escape of pancreatic secretion or inflammatory exudate into the lesser sac, the foramen of Winslow becomes sealed, and a cyst develops.

The contents vary considerably in their gross appearance. They may be clear and serous, yellow, brown, or black, depending largely on the amount of blood they contain. The chief constituents are inflammatory exudate, liquified necrotic pancreatic tissue, and altered blood. In one of Archibald's cases a reaction for bile was obtained.

Examination of the fluid as an aid to diagnosis is of little or no value. The presence of all three of the pancreatic ferments does not prove that the fluid is pancreatic in origin, for any cyst into which hemorrhage has occurred may contain these ferments. The presence of trypsin in large amount, however, is suggestive of a pancreatic origin. On the other hand many pancreatic cysts contain no ferment.

CARCINOMA OF THE PANCREAS

The only common tumor of the pancreas is carcinoma. Kaufmann found this condition present in 1.76 per cent of autopsies on malignant tumors. It is much commoner in men than in women.

Chronic interstitial pancreatitis is frequently associated with carcinoma. Whether this should be regarded as a cause or an effect it is difficult to say. As in the case of the liver it may be that compensatory hypertrophy of the parenchyma consequent upon the fibrosis may be the starting point of carcinoma.

In at least two-thirds of the cases the tumor occurs in the head of the gland. The affected part is enlarged and as a rule extremely hard. The common bile duct is frequently surrounded by the growth,

with, as a result, a deep, persistent jaundice. The gall bladder is dilated in accordance with Courvoisier's law that obstruction within the duct, as by a stone, leads to a thick-walled shrunken gall bladder with thick walls, whereas obstruction due to pressure from without results in a thin-walled dilated one.

Even when the abdomen is opened and the hard mass in the head of the pancreas is in the hand of the surgeon, it may be difficult or impossible to be sure whether the condition is carcinoma or merely a chronic inflammatory thickening. Even the presence of enlarged glands in the neighborhood is not certain proof of carcinoma, for such enlargement may also be the result of inflammation. Not infrequently the

FIG. 132.—Extreme dilatation of the gall bladder and bile ducts due to cancer of the head of the pancreas.

surgeon has the gratifying experience of closing the abdomen on an apparently hopeless carcinoma of the pancreas, only to find that the patient makes a complete and spontaneous recovery.

The carcinoma is usually primary in the pancreas. Occasionally it may be secondary to cancer of the stomach, gall bladder, or bile duct. Secondary growths are common, and are first seen in the lymph glands and the liver. Numerous minute nodules are often scattered throughout the liver, but without any enlargement of the organ, whereas growths secondary to gastric carcinoma cause bulky enlargment of the liver. Occasionally the metastases are more widespread. In one of our cases not only was the peritoneum covered with small, hard, button-like nodules, but both lungs were studded with

similar growths. These, almost without exception, were situated immediately under the pleura, to which indeed they were attached. The spread was apparently through lymphatic channels. Distant dissemination through the blood stream is of rare occurrence.

Microscopically two varieties are observed, adenocarcinoma and carcinoma simplex. The former arises from the ducts, the latter from the acini. The adenocarcinoma is composed of alveoli lined by cylinderical cells, and often presenting papillary outgrowths. It forms a fairly well-defined tumor, usually situated in the head. The carcinoma simplex is a more diffuse growth, and is composed of masses of cells resembling those of the pancreatic acini, the masses being separated by a fine stroma.

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CHAPTER XXII

THE PERITONEUM

Anatomical and Physiological Considerations.—The peritoneum is a serous membrane lining the abdominal wall and providing a covering to the abdominal viscera. The peritoneal cavity is, in health, merely a potential cavity, and contains only a few drops of serous fluid. In the male it forms a completely closed sac, in the female the Fallopian tube communicates with it by a minute opening, a point of great importance, as by this means a uterine infection may reach the peritoneal sac. The various folds and fossæ of the peritoneum are of great surgical importance, but this is not the place in which to discuss them.

The peritoneum consists of a layer of flattened epithelial cells supported by a small amount of subepithelial connective tissue. Outside there is the subperitoneal connective tissue, which in some places contains a large amount of fat.

The peritoneal sac is a closed sac, apart from the openings of the Fallopian tubes in the female. It used to be regarded as a great lymph space in communication with the lymphatic system, but we now know that that system is itself a closed space, and that there exists no direct communication between the two.

The presence of the *stomata* between the epithelial cells which used to be described in silver nitrate preparations was taken as an indication of ready absorption from the peritoneal sac into the lymphatic system. It is now known that these stomata have no real existence, but are merely spurious products formed by a precipitate of silver. Indeed they may be produced independently of a serous membrane, for, when silver nitrate and a dilute solution of albumen are mixed and allowed to evaporate on a slide, an appearance is seen identical with that of the so-called stomata. For a full discussion of this and other histological questions the reader is referred to Hertzler's recent 800 page monograph on the peritoneum.

Although there is no direct communication by means of stomata between the peritoneal sac and the lymphatic system, absorption occurs very readily. Not only colored fluids but small particles may be removed from the peritoneum in this way. It is generally considered that absorption is largely confined to the upper part of the abdominal cavity, and especially to the diaphragmatic surface. This assumption has led to the adoption of the Fowler position in the treatment of acute diffuse peritonitis. The patient is placed is a sitting position so that the purulent material may collect in the pelvis rather than in the upper abdomen and thus avoid being absorbed.

The basis for this view of peritoneal absorption is the fact that the lymphatics of the diaphragm are so much more easily demonstrated than those of other peritoneal surfaces, and especially the abundance in that position of the fictitious stomata. It is now known, however, that absorption takes place readily from all parts of the peritoneal surface. Dandy and Rowntree have shown that in whichever part of the peritoneal sac toxic substances are placed, the rate and degree of absorption are the same. On theoretical grounds there is no justification for the Fowler position, although empirical observations may have another tale to tell.

The rate of absorption is usually supposed to be hastened by the presence of inflammation. There again exact experimental observations are against the popular view. When phenolphthalein or methylene blue are introduced into the abdominal cavity in the course of a laparotomy, it will be found that the time at which the dye appears in the urine depends upon the nature of the inflammatory exudate; in every case of inflammation absorption is found to be delayed, and when the exudate is very fibrinous and abundant there is practically no absorption.

Although there is no direct communication between the peritoneal and pleural cavities, yet septic and other material may pass indirectly from one to the other. The peritoneal surface of the diaphragm is studded with minute pits into which the membrane dips, and which come into close relationship with the lymphatic plexus of the diaphragm. Occasionally, though by no means frequently, bacteria may succeed in entering these lymphatics, whence they are carried to the mediastinal glands, and in this way the pleura may be secondarily infected. Wilkie has pointed out recently how frequently acute inflammation of the gall bladder is associated with signs of infection (moist râles) at the base of the right lung.

The *omentum* is a specialized portion of the peritoneum which deserves separate mention. Various theories have been suggested as to its function in health, such as protection, fat storage, etc. It has marked absorptive powers, and plays an important part in the removal of bacteria and foreign substances. Indeed it has been shown that when bacteria are injected intraperitoneally in not too large quantities, none may be found in the peritoneal fluid at the time of death, and yet abundant cultures may be obtained from the omentum. This explains in part the frequent sterility of a peritoneal exudate, even when the condition proves fatal.

Rutherford Morison, in his Introduction to Surgery, has some excellent remarks on the functions of that abdominal policeman the omentum, from which the following is taken. "It travels about in the abdomen with considerable activity, and is attracted, by some sort of information, to neighborhoods in which mischief is brewing. It may effect a radical cure of hernia, by blocking the hernial orifice with an omental plug. It surrounds, and adheres to, a recently reduced strangulated and damaged loop of intestine; and may keep it alive

and prevent a leak. It is generally found in the neighborhood of a diseased or inflamed appendix; by wrapping it up if gangrenous, or by blocking up the pus from an appendix abscess, it may prevent general peritonitis. In a similar manner it may prevent the perforation of an ulcerating malignant growth, of a gastric ulcer, or the death of a damaged portion of bowel, or the perforation of a suppurating gall bladder. When it is found covering and closely enveloping an ovarian cyst or a fibroid tumor of the uterus, even though not adherent, it is

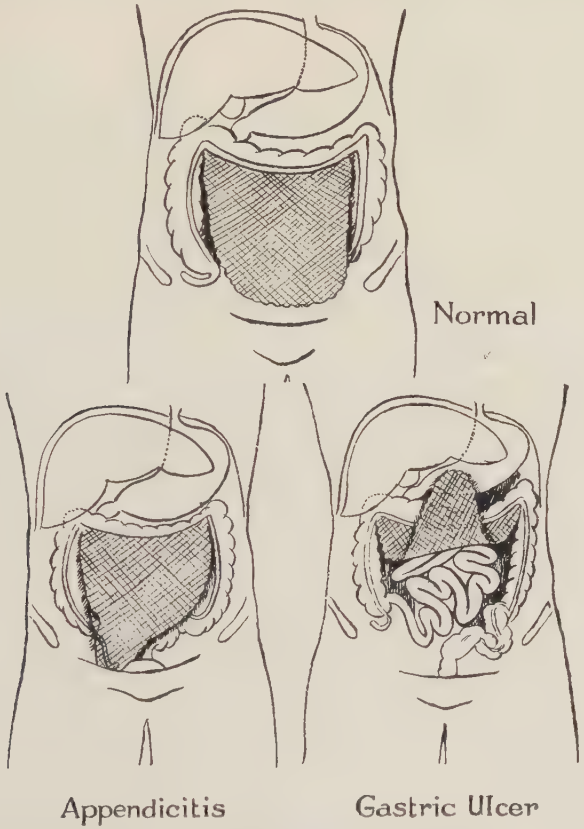

FIG. 133.—To illustrate the protective function of the omentum. (After Rutherford Morison.)

safe to assume that something wrong will be found in the tumor. Its effective mobility is shown by the fact that, whether the lesion be in the diaphragmatic roof of the abdomen or on the floor of the pelvis, there the omentum can and does find its way."

The important diseases affecting the peritoneum are acute and chronic inflammation, tuberculosis and malignant disease; other rarer conditions are hydated cysts and actinomycosis.

ACUTE DIFFUSE PERITONITIS

The cause of acute peritonitis is that of inflammation elsewhere, namely the presence of a irritant. In the vast majority of cases this irritant is bacterial in nature. Passing consideration may, however, be given to *non-bacterial irritants.*

The presence of a foreign body such as a strip of gauze or a drainage tube will give rise to a peritonitis, which usually remains localized. An effusion of blood, such as that from a ruptured tubal pregnancy, will act in a similar manner. So will the escape of fluid from a cyst, a dilated gall bladder, etc.

Even in these cases, however it is doubtful if we are dealing with a strictly aseptic peritonitis. Dudgeon and Sargent have shown that in these cases, and especially in hemorrhagic effusions, the staphylococcus albus can usually be demonstrated. Its presence appears to be beneficial rather than injurious, for it provides the stimulus necessary for the accumulation of phagocytes without giving rise to a progressive inflammation.

Of the *bacterial irritants* the commonest is Bacillus coli, with the streptococcus a good second. Less frequent are the staphylococcus, the pneumococcus, the gonococcus, Bacillus pyocyaneus, the typhoid bacillus, and certain anerobic bacilli. The infection is frequently not pure but mixed.

Infection may reach the peritoneal cavity in three ways:

(1) From the exterior by an accidental wound, or it may be in the course of an operation. Those cases in which the infection, puerperal, pneumococcal or gonococcal, passes along the Fallopian tube to the peritoneal cavity are included in this group.

(2) From the alimentary canal, one of its derivatives such as the pancreas or gall bladder, or an adjacent organ such as the kidney.

(3) From the blood stream. This, by far the rarest method, is seen in one type of pneumococcal peritonitis.

The prognosis of the disease varies greatly, depending on three factors; (1) the virulence of the bacteria, (2) the resistance of the patient, and (3) the source of the infection. Regarding the first it may be said that the streptococcus is the most virulent of the invaders, the bacillus coli may be relatively harmless or on the other hand may be quite virulent, and the pneumococcus usually produces a fatal infection. The second is an imponderable quantity. The source of infection is an important factor. Peritonitis secondary to ruptured duodeneal ulcer or ruptured typhoid ulcer runs a rapid and fatal course. Speaking generally, infections in the upper part of the abdomen are more likely to end fatally than those in the lower part.

Peritonitis commences locally. It may remain local, or may spread and become diffuse. At first the peritoneum simply looks pinker and more injected than normal. Then the normal sheen is lost, owing to the deposition of a thin layer of fibrin on the surface, which acquires

a frosted or ground-glass appearance. The affected part becomes sticky, and the coils of bowel are gummed together.

Microscopic examination shows the usual appearance of an inflamed membrane. The epithelial cells are at first intact, but later may become desquamated. The exudate consists mainly of fibrin threads, with a variable number of leucocytes and it may be some red blood cells. As the disease advances both the exudate on the intestinal wall and the fluid exudate become entirely purulent.

At this stage one of three things may occur. (1) The disease may end by resolution. (2) Adhesions may be formed which keep the inflammation strictly limited. (3) The infection may spread diffusely.

FIG. 134.—Acute peritonitis. Coils of bowel intensely congested and covered with a fibrinous exudate.

These are the three fundamental possibilities of the inflammatory process already considered in Chapter III, namely, resolution, repair with fibrosis, and suppuration with tissue death.

The amount of fibrin deposited depends somewhat upon the infecting organism. In B. coli cases a thick matting is often deposited on the coils of bowel, binding them together in a naturally defensive reaction. In streptococcal cases, on the other hand, fibrin is often very scanty, with little or no matting; this, however, is by no means an invariable rule. During an operation no attempt should be made to

strip flakes of fibrin from off the bowel, for the phenomena of peritonitis are essentially protective. The fibrin forms a protective covering, limits the spread of the disease, and when it is removed a raw surface is left from which septic absorption may readily occur. For the same reason only the gentlest manipulations are allowable.

In the meantime a fluid exudate is collecting. During the earliest stages this exudate is serous, but it soon becomes cloudy and more or less purulent, owing to the admixture of leucocytes and bacteria. The degree of purulence is an index of the resisting powers of the patient rather than of the virulence of the infection. The abdomen may be bathed in thick, creamy pus with little constitutional disturbance. A thin, more or less serous, and possibly blood-stained exudate with only an occasional floating flake of fibrin is very suggestive of a streptococcal infection associated with low powers of resistance and a very bad prognosis. The exudate may be purulent at the site of origin of the infection, but still serous at some distance away. Occasionally there may be a hemorrhagic effusion, due usually to such conditions as twists, strangulation, and thrombosis, in which there is great circulatory disturbance.

If the infection begins to spread, two main channels will be followed. (1) The bacteria may be spread over the surface of the peritoneum by the movement of the bowel. This is prevented to some extent by the protective, policeman-like behavior of the omentum, and by the numerous adhesions which are usually set up. (2) They may spread rapidly and extensively along the lymphatics in the subperitoneal connective tissue, much as erysipelas spreads along the lymphatics of the skin. This method is best seen in streptococcal peritonitis, where the infection may spread like wild fire.

Thrombosis of the mesenteric veins and those in the wall of the bowel is apt to occur when the inflammation reaches them. One result is the possible development of gangrene in a part of the bowel. Another is the ready passage outwards of the bacterial flora of the bowel, producing a mixed infection and great aggravation of the condition. Even comparatively mild degrees of inflammation may render the intestinal wall permeable to the bacteria in the gut.

In cases which recover the removal of all traces of inflammation is as a rule remarkably complete. Not only are the fluid exudate and fresh fibrin absorbed, but even firm fibrous adhesions are dealt with in a surprisingly effective manner. An abdomen filled with adhesions may be found to be almost completely free if opened again at the end of a few months. Here and there, however, fibrous bands may be left as an evil legacy to plague the unfortunate one for many a day.

Although adhesions are usually dealt with in a wonderfully satisfactory manner by the peritoneum, there are cases in which a chronic adhesive peritonitis is the main pathological condition. No organisms may be discovered at any stage, but the condition must be due to some low-grade bacterial infection. At the same time there seems to be an element of personal idiosyncrasy, for in some patients the

abdomen, for no apparent reason, will become filled with adhesions on an even grander scale each time that an attempt is made at their removal.

The general features of acute peritonitis having been described, a word or two may be devoted to the different bacteriological varieties.

Bacillus coli peritonitis is the commonest variety. The organism is usually derived from the gastrointestinal canal, owing either to perforation or to the outward passage of the germs through an inflamed bowel wall. The common source is an inflamed or perforated appendix. An inflamed gall bladder, pancreas, or other organ which may harbor the colon bacillus may be the starting point.

The exudate is abundant and purulent, more especially so in the neighborhood of the starting point of the infection. A large amount of fibrin is deposited on the peritoneum, and floats in the form of flakes in the fluid. A very characteristic fecal odor is noticeable when the chief seat of the trouble is approached. This odor, however, is not present in every case.

This variety of peritonitis is one of the less fatal and fulminating forms, especially when the infection is a pure one. Much more often than is suspected, however, the infection is mixed. An apparently pure culture of the luxuriantly growing colon bacillus is obtained, but the more delicate germs which are really doing the harm may be quite swamped. The earlier in the disease the culture is made, the more frequently will streptococci be found to be present. The culture should therefore be planted by the surgeon at the time the abdomen is opened, and cover-slip smears should always be made. Those cases which are due to perforation of the intestinal wall will of course always present a very mixed infection.

One variety of B. coli peritonitis deserves special mention, namely that which follows upon abdominal operation. It runs an unfavorable course, and is not benefited by reopening the abdomen. Moreover the symptoms so characteristic of peritonitis—fever, pain, and rigidity—are usually absent, yet the patient rapidly goes down hill.

Streptococcal Peritonitis.—The streptococcus pyogenes is the most virulent although fortunately not the commonest of the causes of peritonitis. It may reach the abdominal cavity by any of the methods above mentioned, that is to say from the alimentary canal, from neighboring organs, especially the Fallopian tubes, from the exterior, or by the blood stream. Perhaps the two most important sources are puerperal sepsis and infection introduced from without.

The rapid spread of the disease, more particularly in the puerperal form in which the infection creeps along the tubes, is due to a subperitoneal cellulitis which may sweep the abdomen from end to end. Moreover the cells of the exudate appear to have none of the phagocytic power which they manifest in the B. coli form.

The exudate is thin and watery, only slightly purulent, lacking in odor, containing no flakes of fibrin. The deposit of fibrin on the peritoneal surface is comparatively slight, and the coils of bowel are

not gummed together. This, no doubt, is another reason for the rapid spread of the infection. Cover-slip preparations show numerous chains of cocci.

Pneumococcal Peritonitis.—One of the most serious of the acute abdominal emergencies of childhood is pneumococcal peritonitis. It is true that it sometimes affects adults, but this is of such rare occurrence that the disease may be looked upon as one of childhood and youth.

The pneumococci might reach the peritoneum in three ways: (1) Through the blood stream from some distant focus such as the middle ear. This is generally regarded as the only important route. (2) Through the diaphragm from a pneumonia or empyema. (3) Through the female genital tract, which is usually regarded as a very rare occurrence. The disease is at least three times as common in girls as in boys, a peculiar sex distribution which has hitherto been unexplained.

A very important article by J. R. McCartney and John Fraser appeared in the British Journal of Surgery, April, 1922, which throws a flood of light on the subject of pneumococcal peritonitis. Their main conclusions are as follows.

The disease may be divided into two main groups, primary and secondary. In the primary group the peritoneal inflammation is the original manifestation of the disease. In the secondary group the peritonitis is a development secondary to a previous pneumococcal infection elsewhere, such as a pneumonia or an empyema. No mystery surrounds the secondary form, and it is with the primary form alone that the paper and these conclusions deal.

Primary pneumococcal peritonitis occurs only in the female. Amongst 56 cases McCartney and Fraser did not find a single example in a boy. All the male cases were clearly secondary. Diarrhea, one of the most constant features of the primary form, is never seen in the secondary variety. The disease is almost confined to the poorer classes; other pneumococcal infections are not. Infection is not carried to the peritoneum by the blood stream. It is true that pneumococci are found in blood culture, but they have been absorbed from the peritoneum, just as the recent work of Brown and Cecil has shown that the pneumococci in the blood in pneumonia are absorbed from the lungs. The infection reaches the peritoneum from the genital tract through the Fallopian tubes. At operation the fimbriæ were seen to be congested, and muco-purulent material could be expelled from the interior of the tubes. At autopsy the tubes showed catarrhal inflammation and pneumococci were found in every instance. Careful search for other foci of pneumococcal infection especially in the middle ear, gave negative results. The disease commences as a pelvic peritonitis; in the early cases laparatomy shows a much heavier infection in the lower than in the upper abdomen, and in one case pneumococci were found in the vagina and the pouch of Douglas but not elsewhere, although they were present in the blood stream. In

another instance Type I pneumococci were isolated from the abdomen, vagina, and blood stream, whereas pneumococci obtained from the throat were of Type IV. An analysis of the age incidence shows that the great majority of cases occur between the third and seventh years, and in particular in the fifth and sixth years. In this connection there are two interesting points: (1) it is often only after the third year that epithelial separation of the walls of the vagina is fully established: (2) up to the period between the seventh and eighth years the vaginal secretion is alkaline, whilst after that period it becomes acid and presents a barrier against infection. At operation the peritoneum is seen to be congested and plum-colored. In the early cases the only lesion found is a thin film of exudate over the pelvic viscera. After twenty-four hours the exudate becomes watery and profuse, and contains flakes of fibrin. It is not until the fourth day that it becomes definitely purulent, for the virulence of the infection does not encourage an emigration of leucocytes.

Gonococcal Peritonitis.—This form occurs as a complication of gonorrhea. It is of course very much commoner in females both adult and children, but it may occur in males from infection of the seminal vesicles. In the female the infection is due either to a spread of the disease along the Fallopian tube and through the ostium, or to the rupture of a gonorrheal pyosalpinx.

The peritonitis which ensues is usually confined to the pelvis, although it may become general. Moreover, although acute for a short time, its characteristic manifestations are chronic in nature. A plastic exudate is formed which gives rise to very dense adhesions which bind the pelvic contents into a matted mass, and cause much chronic pain and disturbance of function.

Peritonitis Due to Anerobes.—Although the part played by anerobic bacilli in the production of peritonitis is usually belittled, they may produce a fatal peritonitis. I once had the opportunity of observing a series of cases of anerobic infection following operation on the intestinal tract in which the patient developed symptoms of shock a few days after the operation; the skin was moist and clammy, the pulse running and thready, the temperature moderately elevated, and the features drawn and anxious. The visceral peritoneum was injected, and the fluid exudate was watery and blood-stained, but at autopsy there was very little local change. No anerobic organisms were present in these cases, but Bacillus welchii was found in smears and cultures both during life and at autopsy.

LOCALIZED PERITONITIS

Instead of being diffuse in its distribution the peritonitis may remain localized, so that a collection of pus is formed at and confined to one spot. This limitation is due to peritoneal adhesions, protective in character, which shut off a pocket from the general peritoneal sac. The anatomical folds and cul-de-sacs are naturally common sites for such collections.

The commonest variety is the periappendicular abscess which is walled off so securely that the infection can spread no further. Inflammation of the Fallopian tubes, or of the gall bladder, or the presence of a gastric or duodenal ulcer may be associated with local purulent collections. The pus may eventually reach the surface and discharge there, or the abscess may burst into the general peritoneal cavity or into one of the hollow viscera. In old-standing cases the bacteria may die out and the pus become sterile. One of the most important forms, and one which demands separate consideration, is subphrenic abscess.

Subphrenic Abscess.—A collection of pus between the diaphragm and liver on the right side, the diaphragm and stomach or spleen on

FIG. 135.—Abscess ascending to the right of the colon and extending upward into the subphrenic space. (Keen's Surgery.)

the left, is known as a subphrenic or subdiaphragmatic abscess. The pus usually originates in the upper part of the abdomen, but pus from an appendix abscess or a pelvic abscess may be drawn by the respiratory movements to the region below the diaphragm.

A third of all the cases are due to perforation of a gastric or duodenal ulcer, then come appendicular abscess and abscess or hydatid

disease of the liver; finally there is a miscellaneous group of inflammatory lesions in the kidney, bowel, pelvic organs, pleura, and lung.

The gastric cases occur on the left, the duodenal and appendicular cases on the right side. The abscess is usually intraperitoneal. It may be outside the peritoneum in hepatic cases, renal cases, and those cases of appendicular abscess in which the infection spreads upwards in the cellular tissue behind the ascending colon.

The abscess may contain only pus, or pus and gas combined. The gas may be derived from a hollow viscus, or may be a result of bacterial decomposition. An abscess on the left side nearly always contains gas derived from the stomach. The chief infecting organism is B. coli.

The physical signs may be complicated by an upward extension of the process through the diaphragm giving rise to a serous pleurisy or an empyema. If gas is present in such a case it is possible to distinguish four zones superimposed one on top of the other, as follows: (1) A zone of lung resonance, (2) A zone of pleural effusion dullness, (3) A zone of gas resonance, (4) A zone of abscess dullness. The diaphragm is displaced upward on the affected side, as may be beautifully demonstrated by the X-rays, and the liver may be pushed downwards.

A subphrenic abscess is a steadily progressive condition. The abscess may burst into the pleural or the pericardial sac, or into the general peritoneal cavity.

TUBERCULOUS PERITONITIS

Tuberculosis of the peritoneum is commonest in children and young adults. It may occur, however, at any age, and Osler considers that there are more cases over than under the age of twenty.

As regards sex the statistics vary, depending upon whether they are operative or post mortem. The former show females to be more frequently affected, the latter males. This may be because females come more frequently to operation, but less frequently to autopsy.

The disease may appear in either of two great forms, acute miliary tuberculosis and chronic tuberculosis.

Acute Miliary Tuberculosis of the Peritoneum.—This is merely a manifestation of a general miliary tuberculosis, usually secondary to tuberculosis of the lungs. The local condition is often overlooked owing to the dominance of the constitutional symptoms, or it may be mistaken for typhoid fever. The patient is likely to die of tuberculous meningitis.

Chronic Tuberculous Peritonitis.—For practical puposes the disease may be regarded as always secondary to some tuberculous focus elsewhere, although it is conceivable that the bacilli might pass through the wall of an inflamed bowel and infect the peritoneum.

There are three chief sources of infection: (1) tuberculous ulceration of the bowel, (2) a tuberculous mesenteric gland, and (3) tuberculosis of the Fallopian tube. The last named is one of the most important sources, and is responsible for a large number of the cases in

females. It often happens that the peritonitis persists in spite of treatment, until the tube which is a constant source of reinfection is removed.

Apart from these principal sources the infection may spread from the lung or pleura by way of the lymphatics, or from a distant focus in the bones, joints, or bronchial glands by way of the blood.

Chronic tuberculous peritonitis manifests itself in two main forms. (1) a moist form, in which there is marked fluid exudation, so that this variety is often called the exudative form, and (2) a dry form, characterized by the formation of adhesions and matting of the viscera, often known as the adhesive form. Naturally intermediate forms are common, so that there may be a considerable fluid exudate with numerous adhesions. On the whole, however, the exudate appears to inhibit the formation of adhesions. The exudative form is more characteristic of an acuter infection, as the toxins present do not favor fibrous formation.

The Moist Form.—The disease comes on insidiously, the patient loses strength and weight and wastes away, the abdomen becomes progressively enlarged. In the late stages the clinical picture is very striking, the wasted emaciated frame of the patient, often a child, surmounted by a vast, tense, shiny abdomen over which course numerous distended veins.

When the abdomen is opened it is found to be filled with fluid. This fluid is thin, and of a lemon-yellow or sometimes a greenish color. Its fibrin content is usually low, few or no flakes of fibrin may be seen, but occasionally it may coagulate spontaneously. It often contains some blood, and red cells and lymphocytes are present in the centrifuged deposit. Blood-stained ascitic fluid should always suggest carcinoma or tuberculosis of the peritoneum, although the blood is much more abundant in the former than in the latter. The specific gravity varies from 1.019 to 1.026. The albumen content is between 4 and 7 per cent.

The fluid having escaped, the entire surface of the peritoneum is seen to be studded with fine tubercles about the size of a pin's head. Around and between these there is a varying amount of peritoneal reaction as evidenced by congestion of the vessels and an inflammatory exudate. The latter may in some cases become so abundant as to cover up the tubercles, and eventually cause extreme thickening of the walls of the organs affected.

Not all of the tubercles are miliary in size. Some may be as large as a hazel nut. Masses of enlarged, and it may be caseous, mesenteric glands, impalpable before owing to the presence of the fluid, are often found. The omentum may be greatly infiltrated, thickened, and crumpled up so that it forms a flat mass like a pancake or a rounded one like a sausage which can be felt running transversely across the abdomen. This, however, is more characteristic of the adhesive variety.

A tuberculous lesion may be found, and should always be looked for, in the tubes and ovaries. It is important, however, not to mis-

take the small subserous cysts so frequently seen on the exterior of the tubes for miliary tubercles, an error easily committed by the uninitiated. The lack of any reaction around them and their transparent character readily serve to distinguish them from true tubercles.

The encysted form of tuberculous ascites is usually found in women, but is much rarer than the diffuse variety. The condition is due to a combination of the dry and moist forms, the fluid becoming localized by the formation of dense adhesions. It is of considerable clinical importance, as it is so readily mistaken for an ovarian, parovarian, or other abdominal cyst.

The Dry Form.—In this variety there is little or no effusion, the main characteristic being the formation of a dense inflammatory exudate with numerous adhesions and great matting of the viscera. Even in the fluid form there may be some tendency towards the formation of adhesions.

The deposition of fibrin most readily occurs when there is just enough fluid to fill in the spaces between the sulci, and when the infection is not sufficiently severe for much toxin formation. Although the adhesions become organized they are seldom converted into fully formed fibrous tissue, for when stained by Van Gieson's method they continue to take the picric acid rather than the fuchsin stain.

The coils of bowel are inextricably matted together. The surface may be studded with tubercles, or they may be obscured by the exudate, which often causes such great thickening that they may be confined to the subperitoneal tissue, no tubercles appearing on the surface. This is most marked when the primary area of infection is limited, and is best seen in the region of the cecum and the appendix.

The pancake thickening of the omentum is particularly marked in this form. Caseous masses of considerable size may be formed. A fecal fistula is of fairly frequent occurrence This may be formed by a loop of bowel becoming adherent to the abdominal wall, and ulceration destroying both the wall of the bowel and the abdominal parietes, or a caseous focus may ulcerate into the bowel, and later establish a second communication with the surface. In children the fistula often opens at the umbilicus.

The *prognosis* is not so gloomy as that held by the older writers ("la terminasive constante des affections tuberculenses de peritoine est le mort"—Aran), nor yet is it so rosy as some recent surgical statistics would imply. Opening the abdomen and draining the fluid does indeed produce a wonderfully beneficial effect in the cases with ascites, although the exact mechanism of the improvement is by no means clear. Many such cases, however, although hailed as surgical cures die later of tuberculosis elsewhere. Much depends on the possibility of removing the primary focus. When this is in the Fallopian tube excellent results have been obtained. Conservative treatment alone is successful in a number of cases. Surgical treatment is of course demanded for such complications as intestinal obstruction and abscess formation.

TUMORS OF THE PERITONEUM

Various forms of primary new growth of the peritoneum have been described, of which the most distinct is the endothelioma. These tumors are so rare and doubtful that they need not detain us here.

In considering tumors of the peritoneum it will be convenient to include a number of conditions affecting neighboring structures, especially tumors of the retroperitoneal tissue. The commonest and most important tumors are those secondary to carcinoma of the abdominal organs.

Carcinoma.—Carcinoma of any organ in the abdomen or elsewhere may set up metastases in the peritoneum. The commonest source is the stomach, the next most common is the ovary. Ascites is a frequent accompaniment, and the fluid is usually blood-stained from hemorrhage. Large epithelial cells may occasionally be found in fluid obtained by puncture. These may suggest malignancy, as in tuberculous ascites the chief cell is the lymphocyte.

The disease may spread in three distinct ways, so that three varieties may with convenience be distinguished: (1) by direct extension, as in scirrhous or colloid tumors of the stomach and bowel; (2) by superficial dissemination, as in papillary cystadenomas of the ovary and some cancers of the stomach; (3) by the blood stream, as in diffuse carcinomatosis.

Direct Extension.—Carcinoma of the stomach and bowel usually involves the peritoneal coat sooner or later, and large masses may be formed, particularly in the great omentum and in the gastro-hepatic omentum. When the primary tumor is a colloid cancer the secondary growth may attain a great size, accurately reproducing the original structure.

Extension by Dissemination.—A malignant growth may rupture and disseminate carcinomatous particles throughout the peritoneal cavity. These become implanted on the surface of the peritoneum and may grow to a considerable size, although usually they remain small. Again the original structure is faithfully reproduced.

The best example of this variety is afforded by a papillary cystadenoma of the ovary, the papillary processes of which rupture the capsule and become widely disseminated. A remarkable feature of the condition is that in rare cases removal of the mother tumor may be followed by spontaneous disappearance of the daughter ones.

A carcinoma of the stomach setting up secondary growths in the ovaries does so by shedding cancer cells downwards through the peritoneal cavity. In one of our cases the little nodules could be traced down the peritoneum from the stomach to both ovaries, like the paper scent scattered by the hounds in a paper chase.

A curious variety of this condition is *pseudomyxoma peritonei.* This follows the rupture either of a pseudomucinous cyst of the ovary or of mucous cysts of the appendix. The ovarian cases are by far the more common. Large gelatinous masses, more or less encapsu-

lated, are formed, which may penetrate every part of the peritoneal cavity, even into the space between the liver and the diaphragm, and sometimes produce enormous distension. When the abdomen is opened large globular masses of mucoid material roll out, and can be scraped off the surface of the viscera. The material is so viscid that it can be pulled out into strings and cut off with scissors. It is of the color of honey, and resembles masses of frog's spawn.

The exact mode of production of this material is not certain. Either the tumor cells become implanted on the peritoneal surface, and there reproduce the gelatinous material of the original growth, or the physical presence of the material acts as an irritant to the peritoneum and causes it to react by a further production of similar masses. The former view appears the more probable, but the chief objection to it is that in many cases no cells can be found, and even when they are present they appear ludicrously inadequate to the production of such enormous masses. It must be remembered, however, that in such a condition as colloid cancer where the mucoid material is undoubtedly produced by cells it may be extremely difficult to demonstrate these cells owing to the profound degeneration which is the salient feature of the condition.

The peritoneum shows signs of reaction to irritation. A fine pellicle of fibrin is formed over the mucoid material, which later becomes organized to form a thin vascular membrane. Fine fibrous septa are sent up by the peritoneum between the lobulations of the masses; these branch like a tree and enclose spaces in which the material lies. It is on this account that the masses may prove so difficult of separation. What epithelial cells are present are tall columnar, and show such profound degeneration that it is easy to believe that they will soon disappear.

The *prognosis* is bad. The majority of cases ultimately prove fatal, although it may not be for a number of years. Removal of the primary growth may check the disease, especially when the appendix is the source of the trouble. Recurrence, however, may be expected. Many cases die because of sepsis and embolism.

Extension by the Blood.—Diffuse carcinomatosis, which may have its origin in any epithelial organ, will involve the peritoneum in common with the rest of the body. The entire surface, both parietal and visceral may be studded with small growths. In one such case we found that the metastases were sprinkled as from a pepper pot. These minute metastases are easily mistaken for miliary tubercles, and when the abdomen is opened it may be difficult for the surgeon to decide with which he is dealing. The tubercles are often oblong and may show tiny nodosities on the surface; the carcinomatous nodule, growing expansively, is spherical, free from nodules, but may show slight umbilication. In carcinoma, moreover, there will usually be some masses too large to be called tubercles. The ascitic fluid in tuberculosis contains large numbers of lymphocytes, whereas in malignant disease

large epithelial cells may occasionally be found which will give a clue to the diagnosis.

Retroperitoneal Tumors.—Under this heading it would be possible to include tumors arising from the kidneys, adrenals, pancreas, and other retroperitoneal organs. In practice the term is confined to tumors growing from the connective tissue, particularly that behind the peritoneum of the posterior abdominal wall.

These tumors are of varied character, and are by no means readily collected into groups. We may distinguish the retroperitoneal lipoma and the retroperitoneal sarcoma.

Retroperitoneal Lipoma.—Although this tumor is commonly known as a lipoma it is extremely doubtful if it merits such an innocent name. For it does not consist only of fat; myxomatous areas and even sarcomatous areas may be discovered if a number of different parts of the growth be examined. Extensions existing either as arms of the parent mass or as definite separate growths are not uncommon. At a recent autopsy on an obscure case of paraplegia the pelvis was completely filled by an apparently innocent lipoma. On further investigation it was found that the lipoma was creeping through several of the intervertebral foramina and severely compressing the cord. Only after sections had been cut from many parts of the tumor was one found which showed definite sarcomatous characteristics. There may be firm adhesions to surrounding structures. Finally, removal of the tumor may be followed by recurrence. All these facts go to show that though the tumor may be called a lipoma it should be approached by the surgeon with a very considerable degree of respect. The consensus of opinion, indeed, points to these growths being allied to the teratomata rather than to the innocent lipoma.

The tumor usually appears in middle age, but may begin in early childhood. It is commoner in women than in men. It commences as a rule on either side of the vertebral column about the level of the kidney. Growing very slowly it may reach an enormous size, and be accompanied by profound emaciation of the patient. Almost the entire abdominal cavity may be filled by the tumor. One case is on record in which the tumor was sixty-three pounds in weight. When the abdomen is opened a yellow, lobulated mass of varying size is seen pushing the colon in front of it. It may insinuate itself between the leaves of the mesentery, so as to have the appearance of being primarily a mesenteric tumor. Removal may be easy, or very difficult owing to the adhesions and extensions already referred to.

Microscopically the greater part of the mass consists of adipose tissue, but, as already mentioned, here and there may be found areas of myxomatous tissue and of sarcomatous formation. It appears probable that these have developed primarily and that the tumor represents an embryonal type of tissue, rather than that they are due to a transformation of the lipoma.

Retroperitoneal Sarcoma.—This tumor arises from the fascia of the posterior abdominal wall, usually in the same position in which lipomata

occur. Teratomata, lymphosarcomata, the enlarged retroperitoneal glands of Hodgkin's disease, and sarcomata of the retroperitoneal organs should not be included in this group. It appears probable from recent work that many so-called retroperitoneal sarcomas may really be neuroblastomas (see page 436).

It is a disease of middle life, insidious in onset like the lipoma, and equally difficult of diagnosis. Fixity is one of the chief characteristics both of the lipoma and the sarcoma.

Usually soft in consistence, the smaller growths may be fairly firm. The cut surface is pinkish white. Areas of softening with hemorrhage or cyst formation are common. Microscopically the tumor is a spindle-celled or mixed-celled sarcoma.

CYSTS OF THE MESENTERY

A variety of cystic formations may occur in the mesentery or the omentum. Of these the more important are lymphatic cysts, gas cysts, dermoid cysts, and echinococcus cysts.

Lymphatic Cysts.—These cysts are probably similar in nature to the lymphatic cysts of the neck and axilla, and may therefore be regarded as lymphangiomata of congenital origin. They occur in the earlier years of life, seldom over the age of thirty. Usually single, in some cases a number of cysts may be present. They may be present in any part of the mesentery, but usually in the root. They may attain a great size, but as a rule are no larger than an egg. Their mobility distinguishes them from retroperitoneal tumors, but they may closely simulate an ovarian cyst with a long pedicle.

The wall is composed of fibrous and elastic tissue, and the cavity is lined by a flat endothelium. The contents may be watery, milky, or bloody from hemorrhage. As a rule they are quite clear.

Gas Cysts.—In rare instances there may be gas cysts of the mesentery. These are usually quite small, and they are found clustered along a segment of the bowel. In a specimen in the University of Manitoba Medical Museum the cysts are about the size of a pea. Very similar cysts are of frequent occurrence in the pig. Finney, describing a case of his own, considers that the cysts are probably neoplastic, arising in a connective tissue tumor the cells of which have gas forming properties. Others think that the gas is produced by bacteria. Giant cells with very numerous nuclei (sometimes as many as 50 or 60) may be present, and it is around these that the air spaces are formed. The gas is odorless and does not burn.

Dermoid Cysts.—These may be situated within the layers of the mesentery. More frequently, however, they are retroperitoneal in position. Many of these structures may be called teratoid mixed tumors, and often represent all three of the embryonal layers.

Hydatid Cysts.—Hydatid cysts of the peritoneum or the retroperitoneal tissue are not uncommon. They may form multiple masses of considerable size. Occurring in an Icelander their nature may be

FIG. 136.—Gas cysts of the mesentery.

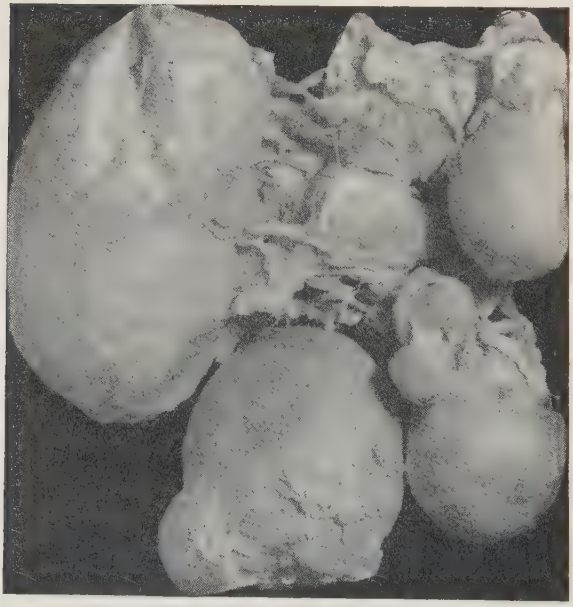

FIG. 137.—Hydatid cysts of the omentum.

suspected, but usually the correct diagnosis is not made until the cysts have been opened and the hooklets discovered.

PERITONEAL ADHESIONS

The formation of adhesions between two peritoneal surfaces is essentially a beneficient process. Without it abdominal surgery would be impossible, the gastro-intestinal canal could never be opened, every local inflammation would become general, every perforation would prove fatal. These remarks are perhaps necessary in view of the attitude sometimes adopted by operators and by the general public towards adhesions, and the tendency to attribute all kinds of symptoms to this cause.

Adhesions may be temporary—they usually are—or permanent. They may be caused (1) by chemical irritation, (2) by mild forms of inflammation, or (3) by mechanical violence.

Adhesions Due to Chemical Irritation.—Almost any chemical irritant, provided it be not too strong, may set up the formation of adhesions. In the days when antiseptics were freely applied to the peritoneal surface adhesions were of frequent occurrence. Iodine is probably responsible in many cases. Suture material soaked in an antiseptic may act in the same way. The escape of the gastric contents as the result of perforation may be attended by adhesion formation at a considerable distance from the perforation.

Adhesions Due to Mild Inflammation.—Adhesions may be found at the site of the pathological lesion producing mild inflammation, or at a distance when the inflammation is more acute. Examples of the former are seen in the adhesions around a gall bladder containing stones, or at the seat of a chronic gastric ulcer. The inflammation spreads outward till it involves the peritoneal coat, fibrin is formed, and fibrous adhesions of a permanent character result preventing the occurrence of such an untoward complication as perforation into the general peritoneal cavity.

When the inflammation is more acute and virulent in character, the exudate is cellular, no fibrin is formed, and adhesions are absent. At some little distance, or it may be a considerable way off, the violence of the process diminishes, and the reparative formation of fibrin becomes possible. At the seat of an appendiceal abscess there may not be a single adhesion, but abundant adhesions may be formed at a distance. A healed gastric ulcer may be associated with adhesions between the omentum and the abdominal wall, and between the gall bladder, liver, and abdominal wall.

The nature of the infecting organism may have an important bearing on the formation of adhesions. The most extreme instances of adhesions are seen in gonococcal infection of the Fallopian tubes. The gonococcus acts as a comparatively mild irritant, and enormous quantities of fibrin may be produced which become converted into permanent adhesions, binding the tubes, ovaries, and uterus into one inextricable mass. The pneumococcus and the staphylococcus excite great fibrin

formation, but the adhesions are more apt to be temporary. The colon bacillus tends to excite fibrin formation, but to dissolve fibrin once formed. The virulent streptococcus renders the protective formation of fibrin an impossibility, so that the infection always becomes diffuse. The presence of digestive ferments will also prevent fibrin formation or dissolve newly formed adhesions.

The majority of what may be called inflammatory adhesions are temporary and disappear when their work is done. Some become vascularized and converted into true fibrous tissue. Even these fibrous adhesions, however, tend to become stretched owing to traction, and to decrease in size. A broad band of adhesion may, when the abdomen is opened again a few weeks later, have shrunk to a mere fibrous cord, which may eventually give way. There is no evidence that, as Lane suggests, adhesions may grow stronger owing to continued traction. An adhesion is merely a scar, and no scar behaves in this way.

Adhesions Due to Mechanical Violence.—A blow on the abdomen may produce sufficient irritation to cause the formation of adhesions. If the violence be sufficiently great, even temporary adhesions may not form, the wall of the bowel becomes necrosed, and perforation a few days later is the result.

The principal cause of permanent adhesions is the injudicious activity of the surgeon. When the peritoneum is incised the cut edges invite the formation of adhesions. It is only when the edges are sutured so that the suture line alone is presented to the peritoneal cavity that this complication can be avoided. An uncovered stump, such as that of the appendix, cannot fail to form adhesions.

If the epithelial layer of the peritoneum is destroyed adhesions are certain to form. For such abrasion to occur a considerable degree of violence is needed. Vigorous rubbing with the finger covered by gauze is insufficient to destroy the continuity. It is true that such rough handling will produce an inflammatory response, but without the formation of adhesions, for the response disappears when the irritant is withdrawn. The omentum is the part of the peritoneum most sensitive to this type of injury.

When the entire thickness of the peritoneum is destroyed, as by means of a cautery, the tendency to adhesion formation on the part of the underlying muscle is comparatively slight.

It is undoubtedly the case that in some individuals there is a peculiar predisposition to the formation of adhesions. As the result of an operation numerous adhesions are formed, which, on being broken down at a subsequent operation, only reform once more. As Hertzler puts it: "This sequence lasts as long as the patient does, or the hopeful persistence of the surgeon endures." Even in a normal person the frayed edges of broken down adhesions form an ideal starting point for the formation of fresh adhesions.

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CHAPTER XXIII

THE UPPER URINARY TRACT

The Kidneys

Anatomy.—The kidney, like the adrenal and pituitary, is of two-fold origin, its two constituents serving different functions and reacting differently in pathological processes. We may speak of these two parts as the kidney filter and the pelvic portion.

The *kidney filter* comprises the glomeruli, the proximal convoluted tubules, the descending and ascending limbs of the loop of Henle, and the distal convoluted tubules. These structures are contained, with the exception of a portion of the loop of Henle, in the cortex. The kidney filter is developed from a mass of cells called the nephrogenic cord.

The *pelvic portion* consists of the collecting tubules, which are contained in the pyramids of the medulla, and the pelvis of the kidney. These, together with the ureter and bladder, are derived from the Wolffian duct. From below they grow up into and invade the nephrogenic mass in a series of rays, the tubules of which become continuous through a wonderful process of fusion with those of the kidney filter. Should such fusion fail to occur accurately the upper set of tubules will end blindly and develop into a series of cysts, a condition known as congenital cystic kidney. In a section of the organ the invasion of the kidney filter by the branching processes of the pelvic portion becomes strikingly evident.

A moment's consideration will show that the kidney filter, with its abundant blood supply, will be specially liable to hematogenous infections, whilst the pelvic portion, with its free communication with the exterior will be more open to an ascending infection from below. It is highly probable, however, that blood borne infection of the pelvic portion plays a much more important part than has hitherto been imagined. In the matter of neoplasms the two parts of the kidney also show a marked difference in behavior.

It is the complexity of kidney structure and the great interdependence of the various constituents on one another that makes what may be termed the medical diseases of the kidney a subject of such difficulty. As the blood supply to the secreting tubules has first to pass through the glomerular capillaries, it is inevitable that a lesion of the glomeruli should implicate the tubules to a greater or lesser extent. The conditions with which the surgeon deals are of a simpler nature, and the chief controversy at the present day centers upon the mode of infection of the kidney, descending hematogenous or ascending ureteric, a question which will presently be considered more in detail.

Tucked away behind the peritoneum and surrounded by a layer of fat of peculiar constitution the kidney occupies a somewhat isolated position in the abdomen. For this reason infection *per extensionem* is of rare occurrence.

There is no province in the whole of surgery in which greater advances in diagnosis have been made within recent years than in diseases of the kidney. This is due principally to two factors: (1) the use of tests for renal function, and (2) the introduction of that instrument of precision, the cystoscope.

Functional Renal Tests.—The experimental production of nephritis in laboratory animals, coupled with the use in such animals of a variety of functional tests has thrown much light on the part played by the glomeruli and the tubules respectively in the production of urine both in health and disease. In surgical work, however, it is sufficient to know the functional capability of the kidney as a whole. For this purpose two chief methods may be employed. In the first a dye is injected and the amount of the dye excreted in the urine estimated. In the second the blood is examined for evidence of retention of those nitrogenous substances which are normally excreted in the urine.

1. *Phenolsulphonephthalein Test.*—A variety of dyes such as methylene blue, indigo carmine, etc., have been used for estimating the excretory power of the kidney, but the one of most general use is the phenolsulphonephthalein test of Rowntree and Geraghty. This consists in the deep intramuscular injection of 1 c.c. of phthalin solution containing 6 mgrm. of the dye. Two glasses of water should be drunk half an hour before the injection, and the bladder emptied just before the dye is given. The urine is collected at the end of one hour and again at the end of the second hour, a few cubic centimeters of a strong solution of NaOH added to each specimen, and the amount of dye excreted is estimated either by means of a colorimeter, or by the simpler method of comparing the color with that of a series of known dilutions of the dye. The healthy kidney should excrete 50 to 60 per cent in the first hour, and 70 to 85 per cent by the end of the second hour.

In surgery the test is principally used to determine the functioning power of each kidney separately. It must not be forgotten that while a reduced excretion of phthalin indicates disease of the kidney (except in conditions of general edema, where the dye may be held in the tissues) a normal amount of dye may be excreted by a profoundly diseased kidney.

2. *Nitrogen Retention.*—Tests for the retention in the blood of nitrogenous substances which are normally excreted in the urine are of more value in Bright's disease than in surgical conditions, since they cannot separate the kidneys as regards function. Under two circumstances, however, these tests are of great use.

(a) When one kidney is nearly destroyed, and we wish to know the excreting power of the other kidney.

(b) In prostatic enlargement when we wish to ascertain if the kidneys can stand the extra strain always thrown upon them when a long-standing source of obstruction is removed.

The two most important non-protein nitrogenous substances in the blood are urea and creatinine. The blood urea normally averages from 12 to 20 mgrms. per 100 c.c., the creatinine 1 to 2.5 mgrms. per 100 c.c. A urea of over 100 or a creatinine of over 5 should be regarded as an absolute contraindication to operation on a prostate which has been the cause of a long-standing obstruction.

Both of the tests are comparatively simple, and require no complicated apparatus. The urea is estimated by adding the ferment urease to 5 c.c. of oxalated blood. The urea is converted into ammonium carbonate by the ferment, and the addition of potassium carbonate drives off the ammonia, which is collected by bubbling through weak acid. The amount of acid neutralized indicates the amount of ammonia produced, and thus the amount of urea present in the blood. The only special apparatus required is a suction pump attached to the water tap.

The estimation of the creatinine is even simpler. The oxalated blood is saturated with picric acid, the precipitated albumen filtered off, 10 per cent Na OH added to the filtrate, and the resulting yellow color compared with a standard of picramic acid or potassium bichromate in some simple form of colorimeter.

The Cystoscope.—The cystoscope gives invaluable information, not merely in disease of the bladder, but also in pathological conditions of the kidney. It serves to determine whether the essential lesion is in the bladder or the kidney. If the latter, it may indicate which kidney is involved, and by its aid the actual type of lesion may in many cases be diagnosed.

In a previous chapter we have seen that a patient may present marked symptoms of stomach disorder, and yet the real seat of the disease may be the gall bladder or the appendix. In like manner the voice of the bladder may drown the feeble complaint of the kidney, so that many a time disease of the bladder is diagnosed when in reality the kidney is at fault.

On the other hand a lesion of the bladder may give rise to renal rather than vesical symptoms. A papilloma of the bladder at the entrance of the ureter may produce obstruction resulting in pain and tenderness in the corresponding kidney, and the hematuria will naturally be regarded as renal in origin.

The most certain means of avoiding these errors is by the use of the cystoscope.

The side affected is indicated by an inflamed condition of the ureteric orifice, or by the passage of pus or blood through the opening.

Finally, the nature of the renal lesion may be indicated by the cystoscopic picture. When a more or less solid pipe of pus is seen to issue from the opening of a ureter it may be assumed that a condition of pyonephrosis exists. A thinner purulent material would point to

a pyelitis or pyelonephritis. Dilatation and rigidity of the opening is associated with dilatation of the ureter and renal pelvis. In tuberculosis the opening often has a characteristic drawn-out tunnel-like appearance, and there may be miliary tubercles in the surrounding mucous membrane. Examination of the urine obtained from each kidney by the ureteric catheter may reveal the infecting microorganism.

A patient suffering from renal disease (apart from Bright's disease) is likely to have one or more of the following symptoms:—

1. Frequent or painful micturition.
2. Pain or tenderness over the kidney.
3. Enlargement of the kidney.
4. Pus in the urine.
5. Blood in the urine.

The conditions most likely to give rise to one or more of these symptoms are:—

1. Suppuration in the kidney.
2. Tuberculosis.
3. Stone.
4. Hydronephrosis.
5. Tumor.

Other conditions to be borne in mind are cysts of the kidney, developmental defects, and perinephritic abscess.

SUPPURATIVE INFECTIONS OF THE KIDNEY

There are three possible routes by which pyogenic bacteria may reach the kidney.

1. By ascent from the bladder and urethra.
2. By descent from the blood stream.
3. By direct extension from neighboring organs, especially from that cesspool of the body, the cecum, the route being along the lymphatics.

As is the way in medicine, first one and then another of these paths has been the favorite of the hour.

For long the ascending route was regarded as the only one worthy of serious consideration. It was pointed out that the pelvis of the kidney was really in direct communication with the outside air, and that, particularly in the female, there was little to prevent pathogenic bacteria from travelling up this path. Later, however, it was recognized that the gonococcus is the only organism which has acquired the art of climbing up the healthy urethra, and that, as has already been seen in the case of the gall bladder, an epithelium-lined duct offers remarkable resistance to such passage.

Direct invasion of the kidney via the lymphatics by the teeming inhabitants of the large intestine has been suggested, but no convincing evidence of this occurrence has ever been brought forward.

It is true that direct extension from a neighboring focus of infection may occasionallly occur, and bacteria may be introduced from without by penetrating wounds, but these are rare occurrences in clinical practice.

To-day the prevailing view is that the common route of infection is by the blood stream, except in stricture of the urethra, enlargement of the prostate, and paralysis of the bladder, in which conditions an ascending infection readily occurs owing to stagnation of the urine.

Descending Hematogenous Infection.—Far from being a rare occurrence it is probable that hematogenous infection of the kidney is comparatively frequent. The kidney is one of the main filters of the body, and any bacteria gaining access to the blood stream are naturally eliminated by this route. There is reason to believe that bacteria are constantly invading the blood stream in small numbers. They are absorbed from two sources:—

(1) Small focal abscesses, notably in the tonsils and at the roots of the teeth.

(2) Mucous membranes in a catarrhal condition, notably the mouth and the large bowel.

These bacteria are carried to the liver and kidney. Three things may happen to bacteria carried to the kidney. (1) They may be destroyed by the renal epithelial cells. (2) If in large numbers they may be excreted in the urine, as in typhoid fever. (3) They may be retained alive as prisoners, in which case alone they will produce inflammation of varying degrees of severity.

Should the inflammation be acute its presence is readily detected. Often, however, it is of such low grade as to betray itself by no clinical manifestation. Such a kidney remains in a damaged condition, and at any time the infection may be lit up, or a fresh infection may be superimposed on the weakened kidney. A similar series of events is well recognized in the case of the appendix and the valves of the heart.

Bacterial infections of the kidney are due to:—(1) the pyogenic cocci, and (2) the Bacillus coli. These attack different parts of the kidney.

The pyogenic cocci involve the kidney filter and produce abscesses in the cortex. They lodge particularly in the glomeruli, where they may form large masses readily seen under the low power of the microscope. Their pathogenicity is high, and they rapidly produce suppuration. The urine, apart from a trace of albumen and a few pus cells and red blood corpuscles, may show little evidence of the severe nature of the infection. It is alkaline in reaction, owing to the ammoniogenic power of the bacteria.

The bacillus coli lodges in the pelvic portion of the kidney, although later the infection may extend into the cortex. The urine is loaded with pus, and is usually strongly acid in reaction. The pathogenicity of Bacillus coli is lower than that of the pyogenic cocci, and a chronic infection may linger for years in the renal pelvis. At intervals recurrent invasion of the kidney from the pelvis may occur, so that in time

the greater part of the kidney may become involved. These invasions may occur along the line of the tubules, but it is more probable that the common route is by the lymphatics in the interstitial tissue.

The overwhelming majority of kidney infections are due to Bacillus coli. In a series of 135 cases examined by Frank Kidd 117 were due to B. coli, 9 to streptococci, 7 to staphylococci, and 2 to the gonococcus.

Ascending Infection.—The only organism which has acquired the power of ascending the healthy urethra is the gonococcus. No organisms can ascend the healthy ureter. Bacteria introduced into the normal bladder quickly disappear and produce no ascending infection.

When there is urinary stasis due to stricture of the urethra, enlargement of the prostate, or obstruction to the ureter bacteria readily make their way from the bladder to the kidney. Theoretically they may do so by three routes:—

(1) By ascending in the lumen of the ureter.
(2) By passing up the lymphatics in the wall of the ureter.
(3) By reaching the kidney through the blood stream.

The obvious route is the intraureteral one. The picture of a bacillus coli swimming up the stream of stagnant urine with vigorous strokes of its flagella is one which appeals to the imagination. It is doubtful if in practice this ever occurs. Even in the case of the infection which so promptly follows implantation of the ureters into the rectum it can be shown that the infection passes up outside rather than within the walls of the ureter.

There is more to be said in favor of the lymphatic route. The mucosa or submucosa of the bladder are supplied with an extensive network of lymphatics which, passing up in the wall of the ureter, communicate with those of the kidney. Bacteria placed on the urethral mucosa pass into the lymphatics and up the walls of the bladder and ureter, congregating in the lymphatics under the capsule of the kidney. From this position, however, they do not infect the kidney nor appear in the urine. Instead, they pass through the lumbar glands, and by way of the thoracic duct they enter the blood stream.

Whatever may be true for experimental infections there can be little doubt that in practice the route of election in ascending infection is via the lymphatics direct to the blood stream and thus to the kidney. The rigor of "catheter fever" is due to the passage of bacteria through the walls of the urethra and thence by the lymphatics to the blood. Although therefore, the infection is in a sense ascending, it is even more truly a hematogenous one.

The question may be asked: If such be indeed the case, why should an ascending infection involve particularly the pelvis and pelvic portion of the kidney? It is because the congestion and consequent lowered resistance of that part of the kidney in urinary stasis render it peculiarly liable to infection by bacteria in the blood stream.

Predisposing Causes of Hematogenous Infection.—When an overwhelming dose of bacteria are presented to a healthy kidney,

resistance is broken down and infection will result. In such a case the infection is always bilateral. When, however, the bacteria are in smaller numbers the existence of some preexisting accessory cause will determine whether or not an infection will be set up, and which kidney will be affected. As Kidd remarks in the opening sentence of his book on Common Infections of the Kidneys, "bacteria are not *the* cause of bacterial infections."

The chief of the accessory causes are retention and trauma.

Retention may be due to a variety of conditions which need not be enumerated here, affecting either the urethra or the ureter. It is not so much the presence of retained urine in the renal pelvis as the congestion consequent upon the damming back which is the factor of importance.

Trauma.—Many traumatic injuries of the kidney of so slight a character as to give rise to no symptoms may predispose the organ to infection by pyogenic bacteria circulating in the blood. Of greater importance is the truma produced by the presence of a stone in the renal pelvis. At the same time it must be recognized that a stone may be the expression rather than the predisposing cause of an infection.

Types of Renal Infection.—In so complex an organ as the kidney it may be somewhat artificial to divide the lesions into separate groups. Infection of the kidney will involve the pelvis, infection of the pelvis will spread into the kidney. For purposes of description, however, it is convenient to consider the following types:—

1. Diffuse suppurative nephritis; the pyemic kidney.
2. Focal suppurative nephritis; septic infarcts of the kidney; pyelonephritis.
3. Pyelitis.
4. Pyonephrosis.

DIFFUSE SUPPURATIVE NEPHRITIS

The lesions in this condition are not confined to the kidney, but are scattered throughout the body. It is merely one manifestation of a general condition of pyemia. Owing, however, to the peculiar anatomical arrangements of the kidney favoring the retention of emboli, in some instances the kidney alone will be involved in addition to the primary source of the infection. That source in many cases is an ulcerative endocarditis, and the infecting organsims are staphylococci or streptococci.

In subacute bacterial endocarditis caused by the streptococcus viridans a peculiar lesion is found confined to the glomeruli, and not proceeding to suppuration.

Both kidneys are always involved in pyemia. During life they are considerably enlarged, red, hot, and steaming. The capsule, which may be tightly stretched, peels off with ease, leaving a surface dotted with minute, opaque, yellowish elevations, each of which is surrounded

by a zone of congestion. These elevations represent minute abscesses, many no more than pin-point in size. The diffuse widespread arrangement should suggest the embolic nature of the infection. In the focal

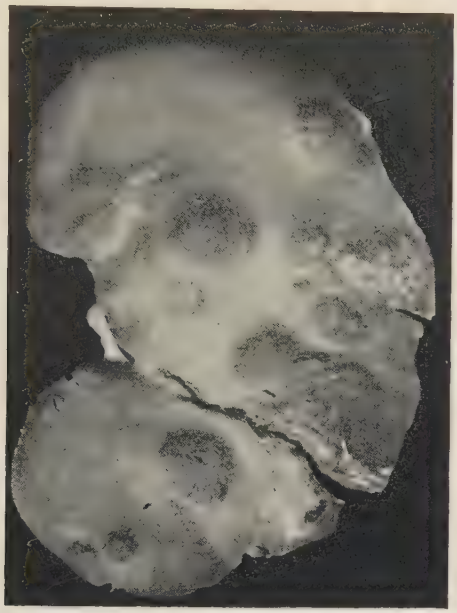

Fig. 138.—Diffuse suppurative nephritis or pyemic kidney.

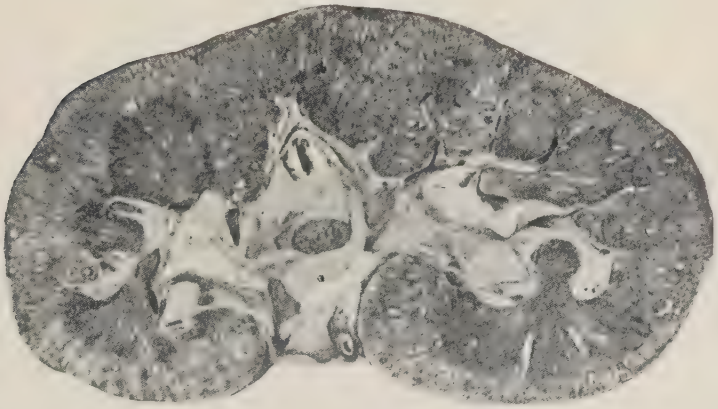

Fig. 139.—Staphylococcus septicemia. Multiple abscesses of the kidney. (MacCallum.)

variety the abscesses tend rather to be arranged in little groups here and there.

On section the surface of both kidneys is sprinkled with numerous minute abscesses. These are most abundant in the cortex, where they are circular in shape. They also occur in the medulla, but there

they take the form of elongated yellowish streaks. The cortex is pale and swollen. The pelvis is seldom affected.

Microscopically, each abscess consists of a mass of polymorphonuclear leucocytes. Masses of bacteria can be demonstrated in the earlier cases occupying the glomerular and the peritubular capillaries. The interstitial stroma in the neighborhood of the abscess shows marked round-celled infiltration. The epithelium of the tubules manifests varying degrees of degeneration and necrosis.

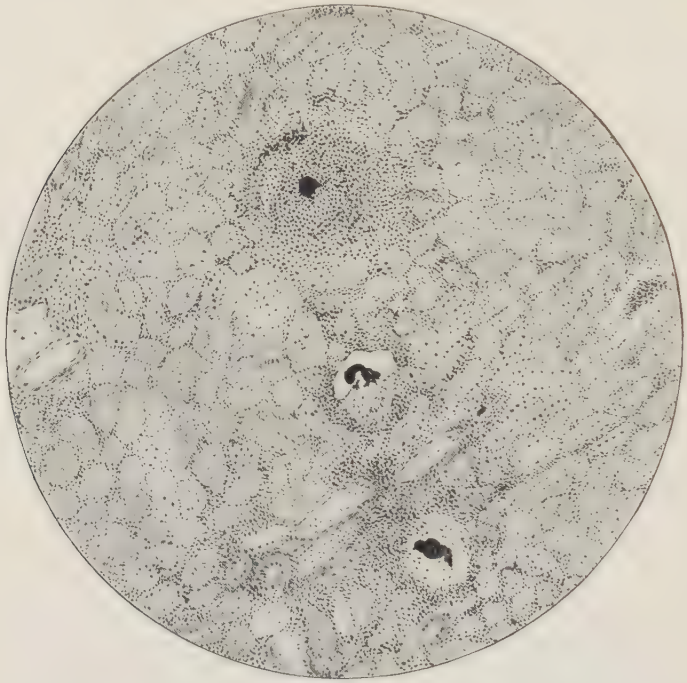

Fig. 140.—Diffuse suppurative nephritis; pyemic abscesses in kidney.

FOCAL SUPPURATIVE NEPHRITIS OR PYELONEPHRITIS

In the pyemic kidney the determining factor is the flooding of the kidney with innumerable bacterial emboli. In the focal variety of suppurative nephritis the determining factor is some local condition which creates a *locus minoris resistentiæ,* and thus renders the kidney liable to infection by bacteria circulating in the blood stream. These bacteria may be the pyogenic cocci, in which case the cortex is mainly involved, with the formation of small abscesses, which tend to spread towards the surface, and which may give rise to a perinephritic abscess.

Much more frequent, however, is infection with the bacillus coli. The bacteria apparently pass through the glomeruli without exciting an inflammatory reaction, but when they reach the collecting portion of the kidney they give rise to abscesses in the medulla and a purulent inflammation of the pelvis. The infection may remain localized to

the collecting portion of the kidney, which is evidently the site of election of the bacillus coli. In many cases, however, the infection gradually spreads upwards in a radiating fashion along the lymphatics, until wedge-shaped areas are formed which have their apex in the pelvis, their broad base at the cortex.

Owing to their distinctive shape these areas have been called septic infarcts of the kidney. They are in no sense real infarcts, as is evident from the above description.

Gross Appearance.—The kidney (and usually only one is affected) is enlarged, and on stripping off the capsule two types of lesion may be

FIG. 141.—Pyelonephritis. The infection is ascending from the pelvis to the cortex.

seen. The first is in the form of small yellow spots representing areas of suppuration. The second and more characteristic takes the form of a dark irregular patch, which proves to be the base of one of the wedgeshaped areas just described.

The cut surface shows one, or it may be many, of these infarct-like areas, separated by comparatively normal-looking kidney tissue. Each area is dark red, but may be mottled with yellow patches of suppuration, which tend to be round in the cortex and linear in the medulla. The pelvis is invariably congested and shows evidence of inflammation.

Microscopically the pyramidal areas show necrosis and great round-celled infiltration. Polymorphonuclears are not so much in evidence as in the pyemic form. The surrounding tissue is intensely congested, and the tubules are markedly degenerated.

The *bladder*, when viewed by the cystoscope, presents, as a rule, well marked changes. In a severe case the whole bladder wall is red, congested, and edematous, presenting an appearance of red velvet. Owing to the edema the usual landmarks are lost. In milder cases the walls of the bladder have a bloodshot appearance, the trigone especially is inflamed and edematous, and here and there may be seen little bunches of pedunculated cysts like small clusters of grapes. The ureteric opening is pouting and congested, so that the side on which the kidney is affected may be readily determined. Cystitis, therefore, is a very common accompaniment and manifestation of pyelonephritis.

PYELITIS

Although a clinical diagnosis of pyelitis is frequently made it will be understood that from the pathological standpoint the infection can never be confined entirely to the pelvis of the kidney, and that the collecting portion of the kidney will always be more or less involved. Often, however, the infection is so predominately one of the pelvis that the term pyelitis may with justice be used. The chief infecting organism as usual is Bacillus coli.

The condition may be acute. In such a case the mucosa of the pelvis is of a bright red color, and is bathed with pus. The walls of the pelvis are swollen and edematous, but no gross change is noticeable in the kidney.

In the chronic cases the pelvis is dilated, the mucosa thickened, and the epithelium flattened or actually ulcerated. A round-celled infiltration of the medulla is gradually replaced by connective tissue formation with atrophy of the parenchyma, so that the condition may come to resemble that of chronic nephritis.

Two varieties of pelvic inflammation are worthy of special mention because of their clinical importance. They are the pyelitis of infancy and the pyelitis of pregnancy.

The *pyelitis of infancy* affects young children, usually under two years of age, and is much commoner in girls than in boys. It is characterized by a high, septic temperature, rigors, and the presence of pus in the urine. The inflammation in the pelvis persists after the acute symptoms have subsided, and there may be pus in the urine for a long time.

The *pyelitis of pregnancy* probably arises from an ascending infection. It does not present any pathological features which differentiate it from other forms of inflammation of the pelvis.

PYONEPHROSIS

This is a condition in which there is extreme dilatation of the pelvis and calyces which are filled with thick creamy pus, associated

with great destruction of the renal parenchyma. The condition may arise in two ways:—

(1) From gradual dilatation of the pelvis due to obstruction, with a superadded suppurative process.

(2) From the progressive destruction of the kidney seen in advanced suppurative nephritis. The latter is more likely to give rise to true pyonephrosis.

The kidney is much enlarged. It is ensheathed in a dense fibro-fatty layer composed of the perirenal tissue transformed by the inflammatory process. This is so adherent that it may be impossible to

Fig. 142.—Kidney in a condition of pyonephrosis. The dilated pelvis is occupied by a large calculus.

strip it off. The surface is irregularly lobulated, and on palpation the lobulations are found to consist of bags containing fluid. When one of these is incised pus of remarkably thick consistence exudes. This pus contains no living bacteria. When the pus is washed away a series of intercommunicating cavities can be seen, representing the dilated calyces which open into the enormously distended pelvis. The renal tissue is thickened to a mere functionless shell, so that the kidney may with truth be called a bag of pus.

The commencement of the ureter shares in the general dilatation. In cases where the ureter is not occluded the cystoscope reveals the very characteristic picture of a worm-like rope of pus uncoiling itself from the ureteral opening.

Microscopically hardly a trace of kidney structure can be recognized. Nothing remains but a confused mass of scar and inflammatory tissue, in which the wreck of a few tubules and glomeruli may now and then be made out.

Rare Conditions.—Two rare inflammatory conditions deserve passing notice.

Pyelitis granulosa is a chronic inflammatory condition which may affect the pelvis, rarely the ureter or bladder. The wall of the pelvis is studded with little red granules which consist of masses of lymphoid tissue. As a rule they produce no symptoms, but may occasionally give rise to one form of hematuria.

Pyelitis Cystica.—The formation of small cysts as the result of chronic inflammation is much commoner in the bladder than in the renal pelvis. The condition is of no pathological importance.

TUBERCULOSIS OF THE KIDNEY

Renal tuberculosis is never a primary condition. This is a self-evident truth, for the tubercle bacillus has no means of gaining direct access to the kidney from without. The lesions to which it is usually secondary are tuberculosis of the lungs, lymphatic glands, and bones. As in the similar case of Addison's disease, however, it may occasionally be impossible to demonstrate with certainty any definite active focus elsewhere.

Tubercle bacilli may be passed out from the blood into the urine by a healthy kidney. It is only when the bacilli are retained in the kidney that disease results. In over 300 cases of pulmonary tuberculosis which came to autopsy at the Phipps Institute, Philadelphia, 82 per cent showed tubercle bacilli in the urine during life. At autopsy, however, in only 40 per cent were there miliary tubercles in the kidneys, and in only 1 per cent was the ulcerative form of tuberculosis present.

The disease may be of two very different types, the acute or miliary form and the chronic or ulcerative form.

Acute Miliary Tuberculosis of the kidney is the renal manifestation of general acute miliary tuberculosis. It may be compared with the diffuse suppurative nephritis of pyemia. It is always bilateral, and rapidly proves fatal, the patient usually dying of tuberculous meningitis. The kidneys are slightly enlarged and studded with minute miliary tubercles, but the condition is not one of interest to the surgeon, and need not be described further here.

Chronic or Ulcero-tuberculosis of the kidney may be compared with focal suppurative nephritis. It is a disease of early adult life, being commonest between the ages of 15 and 40. It is always unilateral at the commencement, and may remain so for a remarkably long time.

Eventually, however, the other kidney is liable to become involved. The very considerable variations in the statistics given in the literature may be explained by noting that when the diagnosis is a post-mortem one the condition will probably be found to be bilateral, whereas a diagnosis made during life will frequently show only one kidney to be infected.

No adequate explanation has ever been given why the condition should at first be unilateral. The kidney cannot be an organ which is specially liable to tuberculous infection, owing to the comparative rarity of the condition. There must be some local predisposing cause.

Fig. 143.—Miliary tubercles on surface of kidney.

A large number of such causes have been suggested, but the arguments supporting none of them can be regarded as satisfactory. It is distinctly remarkable that there appears to be no relationship between stone and tuberculosis.

Route of Infection.—There are three possible routes by which the kidney might become infected:

(1) By the blood stream.

(2) By the lymph stream.

(3) By direct spread from neighboring diseased organs such as the adrenal or the spine.

Whilst it is possible that in rare cases the second and third routes may be that adopted by the tubercle bacillus, in the overwhelming

majority of cases the infection is hematogenous in origin. Tuberculosis of the urinary tract always commences in the kidney. It never begins in the bladder, and then spreads up the ureter to the kidney.

Site of the Initial Lesion.—The primary renal lesion is nearly always in one of the poles, upper or lower, the intervening parenchyma displaying a remarkable degree of immunity. Tuberculous infection parallels in several respects infection by the bacillus coli. In both the infecting agent passes through the kidney filter, settles down in the collecting portion, and then by a retrograde process passes up the lymphatics so as to infect the cortex. In both the urine is acid. The

Fig. 144.—Tuberculosis of kidney showing commencing ulceration.

tendency towards destruction is, however, far greater in tuberculosis than in Bacillus coli infection.

There are two positions in which the process is likely to originate:

(1) In the boundary zone at the base of a pyramid.
(2) In the apex of a papilla as it projects into the pelvis.

To have reached these positions the bacilli must either have traversed the glomerular capillaries and been carried downwards by the intertubular set of capillaries; or, what is more probable, they have been excreted into the capsular space, passed for some distance along the tubule, and there been arrested.

Subsequent Course.—A miliary tubercle composed of endothelial cells surrounded by a zone of lymphocytes is formed in one of the sites just alluded to. The usual necrosis of tissue occurs, and the focus may ulcerate into the pelvis, with early infection of the ureter, and a resulting tuberculous pyelitis.

At the same time a retrograde process commences, the infection creeping up the lymphatics along the line of the collecting tubules, and eventually infecting the cortex and even the capsule. The progress of the infection is evidenced by yellowish-white streaks in the medulla and similar rounded areas in the cortex. Owing to wide-

FIG. 145.—Tuberculosis of kidney. Every stage of the disease is seen from the earliest lesions in the upper pole to the most advanced in the lower pole.

spread infection of the pelvis and calyces the greater part of the kidney eventually becomes involved in this retrograde process.

Gross Appearance.—The appearance of a tuberculous kidney varies greatly with the extent of the lesions and the degree to which destruction has taken place, so that no one description can be given which will be applicable to every case. We may say, however, that in the *early stages* small miliary tubercles or larger yellowish areas may be observed at one or other pole in the boundary zone, the papillæ, or even in the cortex, so that when at operation the capsule is stripped from a

small area of the surface the tell-tale tubercles may be detected, a point of diagnostic value. As involvement of the pelvis occurs at so early a date, the pelvic mucosa will be somewhat roughened and lacking in luster, and the sides of the papillæ may be ulcerated.

The *later stages* are characterized by progressive destruction of renal tissue with cavity formation. The kidney is enlarged, it may be to double the size, and on the surface are to be seen either distinct tubercles or larger bosses denoting cavity formation within.

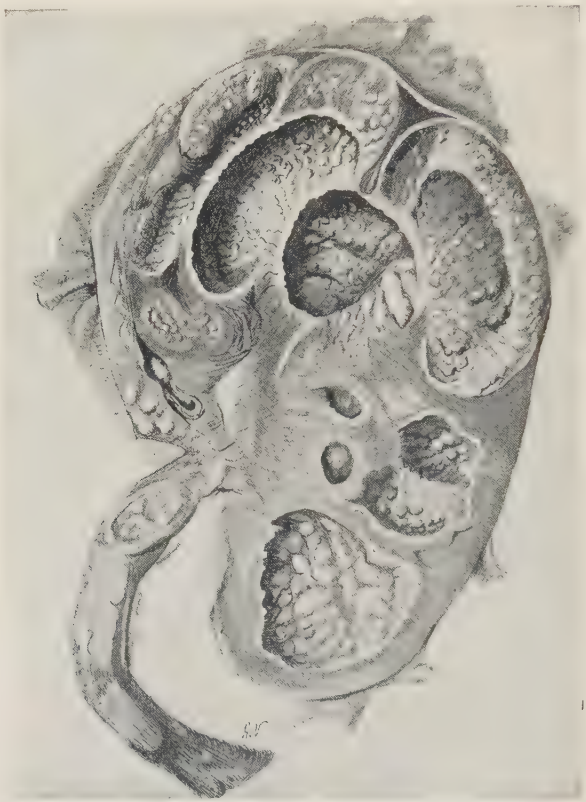

Fig. 146.—Tuberculous pyonephrosis with marked involvement of the ureter.

Where the surface is extensively involved there will be adhesions of the perirenal fat. The cut surface shows:—

(1) Caseous yellow tuberculous masses, notably at the base of the pyramids, and at one or both poles.

(2) Cavities of varying size with rough, ragged walls, containing thick creamy pus without smell and sterile on culture.

(3) Yellowish lines of infection leading up to clusters of tubercles in the cortex.

(4) Extensive ulceration and dilatation of the pelvis with destruction of the papillæ.

(5) Thickening and dilatation of the ureter, although in some cases there may be tuberculous stricture.

One part of the kidney may show early, another part the most advanced lesions. In the late stages a condition of *tuberculous pyonephrosis* develops, and the kidney becomes converted into a multilocular sac, the various cavities opening into a greatly dilated pelvis, and the whole occupied by thick tuberculous pus. In many cases the condition is due to tuberculous stricture of the urethra; in some, however, the essential cause appears to be loss of tone of the musculature of the pelvis and ureter, the ureter being dilated along its entire length.

The final stage is one in which the kidney becomes a functionless mass of tuberculous tissue. The kidney may be enlarged from pyonephrosis, or may be shrunken and atrophic. The ureter is occluded. Lime salts are deposited in the caseous mass, and extensive calcification may occur.

Microscopically the picture depends entirely on the stage of the disease. The early lesion presents the characteristic appearance of a miliary tubercle. As the disease advances the unaffected part of the kidney may show a condition of toxic tuberculous nephritis, due to the action of the tuberculous toxins on the renal epithelium. In the late stages amorphous areas of caseous material are surrounded by tissue which has become so fibrosed that all resemblance to kidney structure is lost.

Healing.—The question of whether chronic tuberculosis of the kidney is capable of spontaneous cure is of great importance from the standpoint of surgical treatment. Partial cure by fibrosis may undoubtedly occur. Outside the fibrosed area, however, it always appears possible to demonstrate small active lesions. At present, therefore, extirpation of the kidney is the recognized method of treatment. At the same time it must be remembered that elsewhere in the body the surgical treatment of tuberculosis is becoming more and more conservative, and in the future the treatment of tuberculosis of the kidney may be less drastic than it is at present. It must be borne in mind that the process is not primary in the kidney, and that at any time the remaining kidney may also become infected.

The Other Kidney.—Renal tuberculosis is at first a unilateral condition. Sooner or later, however, it is most likely to become bilateral. Two different pathological conditions may occur in the other kidney:—

(1) Toxic nephritis of tuberculous origin.
(2) Renal tuberculosis.

The toxic nephritis is due to absorption of toxins from the infected kidney. It manifests itself by the appearance of albumen and it may be of casts in the urine. When the primary source of infection is removed this nephritis speedily clears up.

Tuberculous infection may pass down the ureter from the first kidney, infect the bladder, and pass up the other ureter to infect the second kidney. Or the infection may be hematogenous in origin. The tuberculous toxic nephritis just alluded to weakens the resistance of the kidney, and it succumbs to a blood borne infection. Which of these methods of infection is the commoner it is difficult to say.

The unilateral character of early tuberculosis is well exemplified in the case of a horse-shoe kidney. In this condition there may be widespread infection of one pelvis and yet the other may be quite free. Microscopic examination, however, will frequently reveal the presence of miliary tubercles in the cortex of the other half. These, apparently, are due to infection carried by the lymphatics in the capsule.

Ureter and Bladder.—Tuberculosis of the ureter and bladder is always secondary to tuberculosis of the kidney. It shares in common with other secondary lesions the characteristic that when the primary source is removed the secondary lesion rapidly clears up provided that the disease is not too far advanced.

In the *ureter* the infection passes down in the submucosa. In this layer there may be definite tubercles, or the formation of a diffuse, tuberculous granulation tissue, such as is found in the intestinal submucosa. Ulceration of the mucosa occurs, followed by infiltration and thickening of the muscular and serous coats. The upper and lower thirds are usually much more involved than the middle third. Scar formaton may give rise to stricture, but more often the ureter is converted into a rigid, thickened, and markedly dilated tube.

In the *bladder* infection commences at the opening of the ureter, and spreads along the submucosa of the trigone, giving rise to ulceration of the overlying mucous membrane. As involvement of the ureteric opening occurs comparatively early in renal tuberculosis, cystoscopic examination plays a most important part in the diagnosis of the condition. In the earliest stage there is an irregular area of hyperemia and swelling surrounding the ureteric opening. Later the mucosa becomes thickened and infiltrated, and groups of tubercles or vesicles may be seen. The ureter may appear as a thickened ridge traversing the wall of the bladder, and the opening may project like a crater into the bladder. Ulceration of varying extent develops sooner or later. Even before removal of the kidney many of the bladder lesions show a remarkable tendency to heal, so that healed tubercles may be found in the neighborhood of quite active lesions. Removal of the kidney may be followed by complete recovery.

RENAL CALCULUS

It is convenient in this place to consider the general problem of urinary calculi, whether in the kidney, the ureter, or the bladder. The special characteristics of the various calculi will be described under the headings of the various organs in which they occur.

A urinary calculus is a stone-like body composed of urinary salts bound together by a colloid matrix of organic matter.

It consists of a nucleus around which are deposited concentric layers of one or more of the urinary salts. These salts as they occur in the urine are of crystalline structure. In a calculus, however, the crystalline structure is entirely lost, and all that can be seen is an amorphous mass of granules embedded in an albuminoid matrix. The albuminous material, therefore, occurs not only in the nucleus but in all the successive layers which go to make up the calculus.

Three principal constituents go to the making up of urinary stones: uric acid, calcium oxalate, and ammonio-magnesium phosphate—the so-called triple phosphate. These may occur alone, but frequently they are combined.

Stones have been divided into two groups, primary and secondary.

Primary stone forms in the urine without any antecedent inflammation. It consists usually of uric acid, urates, or calcium oxalate, although in rare cases it may be composed of cystin, xanthin, or calcium carbonate. The urine is acid.

Secondary stone is formed as the result of inflammation. The common constituent is ammonio-magnesium phosphate, but amorphous phosphates and ammonium urate may enter into its composition. The urine is alkaline.

FIG. 147.—Two examples of oxalate calculi.

Uric Acid Stone.—Uric acid is the commonest constituent of urinary stones. It may occur alone, but is usually combined with urates and oxalates. The stone is of moderate hardness, light to dark brown in color, and on section when polished it displays the wavy concentric markings of an agate. It occurs in acid urine.

The oxalate stone may be recognized by its extreme hardness, its dark color due to staining with blood from the injuries it produces, and its peculiarly spiny and prickly exterior, from which it derives its name of mulberry calculus. On section it shows wavy concentric laminæ. It occurs in acid urine.

The phosphatic stone, consisting of triple phosphates, may occur pure, or as a covering of a primary stone. It is white, smooth, soft, and friable. When mixed with other constituents, however, it may be tinged with their color. It occurs in alkaline urine.

Etiology.—The conditions which govern the formation of urinary calculi are still far from understood. The two factors which naturally suggest themselves are a high concentration of crystalline salts in the urine and inflammation in the urinary tract. But the urine may be loaded with crystals for long periods without the formation of stone. Secondary phosphatic calculi in the bladder it is true are a not infrequent accompaniment of the cystitis associated with enlargement of the prostate, but on the other hand inflammatory conditions of the renal pelvis are very common, whereas renal stones are comparatively rare. Moreover pyelitis is much commoner in women than in men, whereas the incidence of renal stone is just the reverse.

In spite of these facts there is evidence that infection and a high urinary concentration of salts are factors which cannot be disregarded. Rosenow and Meisser, working with streptococci from the urine of patients with multiple recurrent calculi, have succeeded in repeatedly producing calculi in the kidneys of dogs by implanting these streptococci in devitalized teeth of the dogs, thus establishing foci of chronic infection. Keyser has obtained equally interesting results by feeding rabbits with oxamide, a diamide of oxalic acid. In 50 per cent of these rabbits there was definite stone formation. The subcutaneous injection of butyl oxalate, an ester of oxalic acid, was accompanied by an intense oxaluria for a considerable time, and by the formation of definite oxalic calculi.

The fusing of urinary crystals into non-crystalline calculi appears to depend on the colloid content of the urine. It is probable that the colloids of the urine normally keeps the water-insoluble crystals such as urates and oxalates from crystallizing out. The presence of an abnormal colloid or an interference with the normal colloids of the urine may cause the normal crystalloids to be precipitated; an undue concentration of crystalloids may under certain circumstances produce the same results. It would appear, however, that not any inflammatory colloid is sufficient to bring about the precipitation, for, as already remarked, pyelitis is very frequently present without any stone formation. It may be, as Rosenow suggests, that certain specific bacteria may be required for the production of stone-forming colloid. It is well known that certain patients have what may be called a stone-forming diathesis; stone after stone may be removed from the kidney, but it continues to produce new ones.

The curious concentric formation of the deposits is not confined to urinary calculi, but is seen also in gall stones, in the corpora amylacea which occur in the prostate and elsewhere, and in the psammoma bodies of the meninges and brain. Although our knowledge of the factors which govern calculus formation in general is still far from complete, the following explanation of the laminated appearance is suggested by the analogy of the behavior of colloids in chemistry and in geology.

When a solution of a salt such as silver nitrate is brought in contact in a test tube with a colloid gel like gelatine to which potassium

bichromate has been added, a process of "rythmic precipitation" sets in and a succession of colored rings are laid down, produced by the union of the bichromate with the silver salt as it gradually penetrates the gel, which acts as a semipermeable membrane. Calcium salts in solution have a similar power of producing rythmic precipitation in a gel. Liesegang has shown that many geological substances which are characterized by the presence of concentric rings, as for instance the agate, are probably formed in this way. It may be that the rings so characteristic of urinary and biliary calculi may also be formed by the gradual action of an electrolyte upon a mass of colloid material with resulting rythmic precipitation.

One of the most remarkable features of primary stone is its *geographical distribution*. In some parts of India and in Egypt it is quite common. In North America, on the other hand, it is comparatively rare.

There can be no doubt that the reaction of the urine has a very important bearing on the type of stone found. A stone may show several layers of uric acid followed by deposits of phosphates. The change is due to an alteration in the reaction of the urine caused by infection with pyogenic cocci which are ammoniogenic. Subsequent infection by the bacillus coli may bring back the urine to acid, with the deposition of calcium oxalate.

Stone in the Kidney.—A stone in the kidney is formed in the renal pelvis. It may remain in the kidney, or may, before it has become too large, pass down into the ureter where it forms a ureteral calculus, or finally it may reach the bladder where it becomes a vesical calculus. Most stones in the bladder originate in the kidney. The condition is much commoner in men than in women. It usually occurs between the ages of twenty and forty. The stone as a rule is single, but occasionally numerous small stones may be found.

A renal calculus is usually uric acid or oxalate in type. The effects produced in the kidney are so variable that they cannot be described in detail. They are dependent on three factors, retention, infection and suppuration. The symptoms depend mainly on the size of the stone. As Cabot puts it," little stones, like little dogs, are likely to make the most noise." The large stone is often a silent stone.

If the stone produces obstruction of the ureter and *retention*, a condition of hydronephrosis is superadded to that of stone. The stone may or may not completely fill the dilated pelvis. In the latter case the stone is usually of the branching or coralline variety. Should the obstruction be complete, anuria will develop, with atrophy of the kidney.

In many cases *infection* develops as the result of the stone in the kidney. The bacteria probably reach the kidney through the blood stream. The effect depends on the condition of the kidney at the time. If there is little or no obstruction the result will be a pyelonephritis. If, however, dilatation has already occurred a condition of pyonephrosis will develop. The infection will naturally hasten the formation of the stone.

Wherever the stone presses on the kidney *ulceration* will occur. In the case of a large stone the effect will be extensive destruction of kidney tissues. In rare cases the stone may ulcerate through the wall of the pelvis or ureter and escape into the abdominal cavity.

Stone in the Ureter.—At any moment a small stone may leave the kidney and enter the ureter. It may traverse the canal and enter the bladder, giving rise to the agony of renal colic. Or it may be arrested in the ureter and lodge there. At the point of arrest the wall of the ureter becomes ulcerated, and later a stricture may develop. The ureter above the obstruction becomes greatly dilated. X-ray studies have shown that ureteral calculus is a much commoner condition than was formerly suspected. Indeed some observers state that ureteral stone is almost twice as common as stone in the kidney.

HYDRONEPHROSIS

Hydronephrosis is a condition of dilatation of the renal pelvis and calyces, with accompanying destruction of the kidney tissue. It is caused by some obstruction to the outflow of urine. This obstruction must be gradual or intermittent. If sudden or complete the back pressure soon induces suppression of urine, so that the dilatation of the pelvis, although present, is very slight in degree.

Etiology.—The cause of the gradual obstruction may be in the urethra, in the bladder, or in the ureter. In the first two instances the resulting hydronephrosis will be bilateral, although usually more marked on one side than the other. In the third it will be unilateral.

In the *urethra* the common causes of obstruction are stricture and enlargement of the prostate. I have seen a case of marked bilateral hydronephrosis the result of a urethral calculus of 30 years standing.

In the *bladder* a calculus acting as a ball valve may produce intermittent obstruction of the urethral opening.

In the *ureter* the cause may be within the ureter, in the wall of the ureter, or without the ureter.

In the lumen of the ureter the usual cause is a rounded ureteral stone, or a renal calculus of conical shape projecting into the commencement of the duct.

In the wall of the ureter an inflammatory process, pyogenic or tuberculous in nature, may cause obstruction of the lumen, or, by leading to the formation of scar tissue, may give rise to marked cicatricial stenosis.

Outside the ureter there may be compression by a tumor, by fibrous bands, by fecal impactions, or by an abnormal renal artery crossing and pressing upon the commencement of the ureter. One of the commonest causes of hydronephrosis is an abnormally movable kidney, which gives rise to kinking of the ureter with the usual result.

Morbid Anatomy.—The essential change in hydronephrosis is dilatation of the renal pelvis. The normal pelvis has an average capacity of 7 to 10 c.c. The dilatation may become so enormous that

the capacity is increased to several liters, and one case has been reported in which there were 36,000 c.c.

As the pelvis and calyces dilate they do so at the expense of the renal tissue. Usually, therefore, both pelvis and kidney are involved. In exceptional cases the kidney for some reason escapes, and appears attached to the sac-like pelvis like some appendage. In still rarer cases only the kidney undergoes dilatation, and it then appears to envelop the pelvis which may be contracted about a stone.

Fig. 148.—Hydronephrosis and dilatation of ureter due to impaction of stone at lower end of ureter.

In the process of dilatation first the pyramids and then the cortex suffers, until finally the kidney becomes converted into a huge lobulated bag of fluid in which only vestiges of the interlobular septa remain. The cortex is thinned to a mere shell. The fluid is clear and watery, and its content of urea, uric acid, and salts is very low. Should infection occur the condition changes to one of pyonephrosis or infected hydronephrosis.

Microscopically there is extreme atrophy of the various elements of the renal tubules, together with an associated round-celled infiltration and interstitial fibrosis. The epithelium lining the tubules becomes flattened, and the glomeruli obliterated and fibrosed. The final sclerosis may be extreme, but even in the most advanced cases small areas may be found where comparatively normal glomeruli and tubules continue to exist.

Pyelovenous Back-flow.—There are certain problems in connection with hydronephrosis which have always been difficult of explanation. How is it that in some cases complete obstruction of the ureter is followed not by anuria but by the development of a marked hydronephrosis, and how is it that the contents of a hydronephrotic sac are not a stagnant pool but rather a fresh water lake? Moreover, even in a case of long-standing hydronephrosis with complete obstruction parts of the kidney may be found to be still in an actively functioning condition. Some form of pelvic reabsorption must occur, thus allowing of a circulation of the fluid within the dilated pelvis.

Hitherto it has been supposed that this absorption must take place by way of the tubules, but of this there has never been any direct

experimental evidence. Hinman and Lee-Brown have now shown by a series of beautiful experiments that the absorption occurs not through the tubules but directly from the pelvis into the veins. By injecting the pelvis with sodium bromide at a pressure lower than the renal secretory pressure they were able to demonstrate in X-ray pictures that there was a pyelovenous back-flow from the minor calyces into the large venulæ rectæ at the base of the pyramids, and that once the communication was established a lower pressure than the initial one was enough to keep it open. In this way they could inject the entire venous system of the kidney as readily as by an injection directly into the vessels. Phenolsulphonephthalein injected into the ureter at an adequate pressure appeared in the urine flowing from the other kidney as quickly as when the dye was injected into the blood stream. The significance of this discovery not only with regard to hydronephrosis but also in relation to the occasional accidents of pyelography can hardly be overestimated.

TUMORS OF THE KIDNEY

The study of kidney tumors is one of the most perplexing and confusing chapters in the whole of pathology. The history of the various conceptions which have been popular at different times is full of interest, but the reader must be referred to the pages of Ewing (to which I am indebted for much of what follows) for a full discussion of the subject. The following brief summary may be given.

At one time all tumors of the kidney were divided into two classes, one in which the tumor arose from the epithelium of the renal tubules, the other comprising yellowish tumors which were regarded as lipomas. In 1883 Grawitz pointed out the close resemblance between these so-called lipomas and the cortical hyperplasia of the adrenal first described by Virchow. Moreover he demonstrated the occasional presence of adrenal remnants or "rests" in the capsule and cortex of the kidney. From these facts he concluded that the fatty tumors were adrenal in origin, being derived from the adrenal rests in the kidney. The tumor was therefore known as a hypernephroma or Grawitz' tumor. Enthusiastic disciples soon included the majority of kidney tumors in this category. In 1893 Sudeck, followed by Stoerk in 1908, attacked the popular conception, pointing out that many of the features supposed to be characteristic of Grawitz' tumor were shared equally with tumors undoubtedly arising from renal tubules. Again the pendulum has swung violently, and many writers now claim that there is no such thing as a hypernephroma, and that all kidney tumors arise from tubular epithelium. As usual the truth is to be found in neither extreme camp. It is true that perhaps the majority of renal tumors are carcinomata of renal origin, but it is also true that there is a well defined class of tumors which are certainly hypernephromata and of adrenal origin. The two groups have many features in common, but we shall see how they may be differentiated.

At the risk of being accused of undue dogmatism for the sake of clearness we may recognize three main types of kidney tumor: (1) the adenocarcinoma of adults, (2) the hypernephroma of adults, (3) the embryoma of children.

Adenocarcinoma.—A large number of the tumors of the adult kidney which used to be regarded as hypernephromata are now known to be adenocarcinomata. They have many points of similarity both in their gross and in their microscopic appearance. The points of difference will be indicated as they arise.

FIG. 149.—Adenocarcinoma of kidney.

Gross Appearance.—In the early stages the tumor is a small nodule of a characteristically light yellow color, which may be found in any part of the cortex or medulla. At a later date it may attain a great size but without appreciably altering the shape of the kidney. It is not well encapsulated, and as it grows it invades the kidney substance and surrounding structures. Portions of compressed kidney tissue are seen here and there at the periphery of the mass. Very characteristic is the presence of numerous cysts. Some of these cysts contain clear

fluid, others gelatinous material, whilst into others hemorrhage has occurred. Close inspection of some of the cysts may reveal evidence of papillary projections. As the tumor increases in size there appear opaque areas of necrosis into which hemorrhage may occur. The picture, therefore, is a most variegated one.

The points in which the gross appearance differs from that of a hypernephroma are: (1) the lack of encapsulation and the general tendency to invade the surrounding renal tissue, (2) the presence of cysts with clear or gelatinous contents, and (3) the gross evidence of papillary formation.

Invasion of the renal veins occurs at an early stage, and the tumor may grow along the renal vein, up the vena cava, and into the right auricle of the heart. Metastases are common and widespread, two of the commonest organs to suffer being the lungs and the liver. Secondary growths in bone are of remarkable frequency, as in the case of hypernephroma.

These tumors, together with true hypernephromata, are sometimes associated with remarkable disturbances of temperature. In one case which I studied the two chief features of the illness were the presence of a lesion in the lung (confirmed by X-rays) and an intermittent temperature over a period of 12 months. A tumor of the kidney was never suspected until a short time before death. Autopsy revealed the presence of a small adenocarcinoma of the kidney with a pulmonary metastasis.

Microscopic Appearance.—When we turn to the histological structure of the renal adenocarcinoma we are confronted by a variety of pictures which is largely responsible for the multitude of current theories on the subject. Without entering unduly into minutiæ we may distinguish two main types of growth, the papillary and the alveolar.

1. The *papillary form* is made up of long villous strands of connective tissue covered by tall epithelial cells, and enclosing narrow sections of tubules into which papillomatous processes project. When we come to study the nature of the epithelium we are forced to make a further subdivision into a large group with clear cells and a small group with granular cells. The *clear cells* are indeed the most characteristic feature of one group of tumors. They are large, and of a remarkable clearness, resembling vegetable cells. They often contain a considerable amount of lipoid together with an abundance of glycogen. In some specimens, however, no reaction for fat can be obtained. There is a superficial resemblance between these cells and those of a hypernephroma, but the cells of the latter will be found to be slightly granular, foamy, and interspersed with lipoid granules. The columnar cells are firmly adherent to the stroma and have a somewhat rigid palisade arrangement in marked distinction to the loose arrangement seen in hypernephroma. It is to the tumor with clear cells that the gross description given above especially applies, and it is it which usually is responsible for metastases in bone.

The papillary adenocarcinoma with *granular cells*, a much rarer tumor, is frequently multiple and appears as light colored nodules in the renal cortex. The nodules are at first miliary in size, and rarely become larger than a pea. They usually occur in sclerotic kidneys. Fatty changes and hemorrhage are lacking, nor is invasion of the renal vein common.

2. The *alveolar adenocarcinoma* forms a small but well defined group. The tumor is made up of well-formed though irregular tubules

FIG. 150.—Hypernephroma. The variegated character of the cut surface is well seen.

and acini, derived from the renal tubules, and separated by a cellular stroma. The acini are lined by cubical or columnar granular cells. Fatty degeneration, necrosis, and hemorrhage are uncommon. The rare form of carcinoma occurring in children (not to be confused with the much commoner embryoma) is of this description.

Hypernephroma.—Although there can be little doubt that a large proportion of the kidney tumors which used to be regarded as hypernephromata are in reality adenocarcinomata, there remains a well defined group which fulfills the requirements of Grawitz' tumor.

In most cases the tumor arises in one of the adrenal rests which Grawitz conclusively showed to lie under the capsule of the kidney. In some cases it originates in the adrenal and invades the kidney. If the adrenal cannot be found the tumor is pretty certain to be a hypernephroma.

Gross Appearance.—The hypernephroma resembles the renal adenocarcinoma in many respects. It forms a large, rounded, encapsulated mass which, in common with other renal tumors, causes comparatively little change in the shape of the kidney. It is often confined to one pole, usually the upper, but may occupy the entire kidney. The two chief characteristics of the cut surface are the yellow color and the remarkably variegated appearance. In the early stages at least a central fibrous area can be distinguished from a more cellular cortical part. Areas of necrosis and hemorrhage are very common, and hemorrhagic cysts formed from the degenerated spots are numerous.

At first the growth is sharply separated from the kidney by a definite fibrous capsule, and in that respect may lay claim to be regarded as an innocent growth. Sooner or later, however, the capsule gives way, and true invasion of the kidney occurs. There is a special tendency to vascular involvement, invasion of the renal vein and even of the inferior vena cava occurs, and widespread metastases is the result, the lungs and the long bones being the principal sufferers. The peculiar sex changes, so characteristic of growths of the adrenal, never occur in renal hypernephromata.

Microscopic Appearance.—The picture varies considerably in different specimens. In some cases the zona glomerulosa or the zona fascicularis of the adrenal cortex is reproduced with tolerable fidelity, the cells being arranged in groups or in long cords. In other cases the cells are arranged in broad sheets, giving a trabecular arrangement. In still others (and these the most malignant) the cells are scattered quite diffusely. The rows or groups of cells are separated by an extremely abundant capillary network, which renders hemorrhage of frequent occurrence. The cells themselves are highly characteristic. They are of large size, and the cytoplasm, although much paler than in ordinary renal cells, is not so clear as in the clear-celled adenocarcinoma, but is slightly granular owing to the presence of numerous lipoid globules and glycogen granules, which impart to it a foamy appearance It contains a large amount of lipoid, an ester of cholesterin, doubly refractive to polarized light. In the true hypernephroma there is no suspicion of papillary or alveolar formation.

The chief points of difference between a hypernephroma and an adenocarcinoma may be summed up as follows: (1) the adrenal tumor shows a central fibrous core and a more cellular periphery; (2) the adenocarcinoma is more markedly lobulated and contains numerous small cysts filled with clear fluid; (3) the presence of lumina is characteristic of adenocarcinoma; (4) the same may be said of a marked papillary arrangement; (5) the foamy cytoplasm of the hypernephroma contrasts with the clear cells of the common type of adenocarcinoma;

(6) in adrenal growths there is a very loose relation of the cells to one another and to the stroma.

Embryoma.—In the older writings the tumors of childhood were classed as sarcomas, although they showed great variations in structure. Recent work has thrown entirely new light on the subject, and

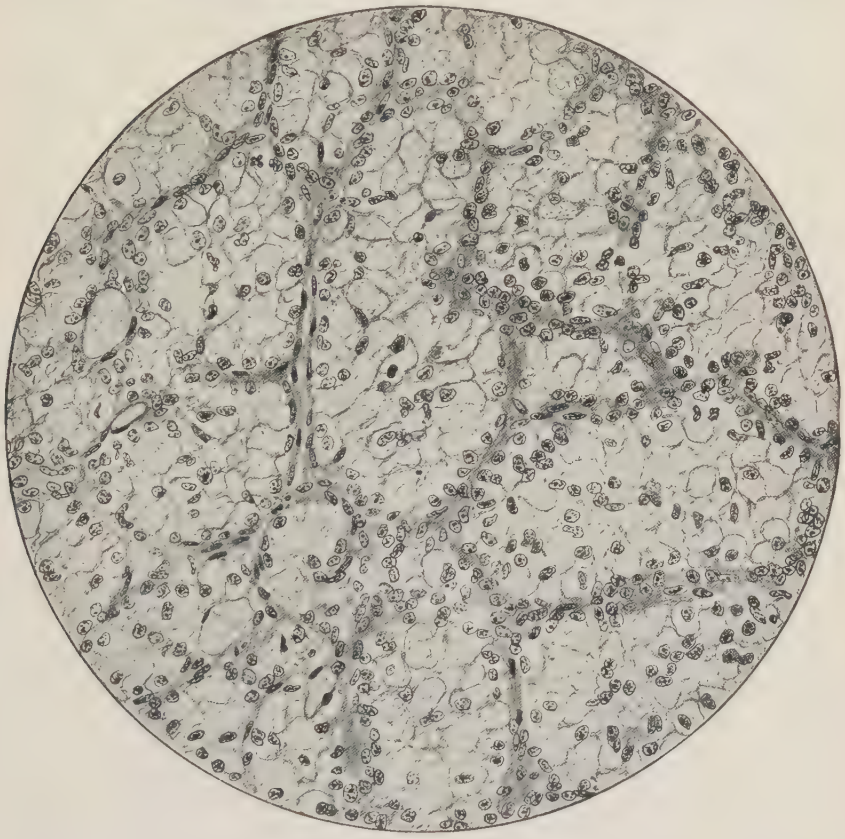

Fig. 151.—Hypernephroma showing characteristic large clear cells. (MacCallum.)

most of these tumors are now regarded as of embryonal type, although other varieties of neoplasm may also occur.

The greatest frequency is between the first and third years, and after the age of five these growths are infrequent, although they may also be met with in adults. There is a curious tendency in children for these tumors to be bilateral, a tendency which, as Bland-Sutton has pointed out, is shared by paired organs such as the ovaries, testes, eyes, and crura cerebri.

Gross Appearance.—They vary greatly in size, being sometimes quite small, but often reaching extraordinary dimensions. Bland-Sutton mentions one case in which the tumor weighed 31 pounds. The growth may commence in the substance of the kidney, usually

at one or other pole, or it may apparently start in the pelvis. Rapid increase in size is the rule, but the ureter is not invaded until later in the disease, which may account for the customary absence of pain and hematuria. The consistance is soft, the color grey or yellowish. Areas of necrosis and hemorrhage are common, and these will naturally alter the gross appearance.

The tumor spreads by invasion of the kidney, or later of the neighboring organs such as the liver, spleen, and intestine. Metastases by the blood stream are not frequent, but may occur.

Fig. 152.—Embryoma of kidney.

Microscopically the appearance is so varied that a detailed description is impossible. It may be sarcomatous in type, round-celled, spindle-celled, or adeno-sarcomatous. More common, however, is the "mixed" tumor. This variety consists of an undifferentiated cellular stroma in which may be found tubules, smooth muscle, striated muscle (rhabdomyoma), cartilage, bone, and fat. The tubules bear no resemblance to normal kidney tubules.

The embryonal tumors of the kidney are of developmental origin. They probably arise from rudiments of the Wolffian body included in the kidney, and the cartilaginous and bony tissue may have its origin in the vertebral anlage.

In most cases the tumor arises in one of the adrenal rests which Grawitz conclusively showed to lie under the capsule of the kidney.

In some cases it originates in the adrenal and invades the kidney. If the adrenal cannot be found the tumor is pretty certain to be a hypernephroma.

Metastases are of frequent occurrence. These, it has already been pointed out, take place by the blood stream. The lungs, therefore, are the common seat of secondary growth. The tumor cells may succeed in passing the pulmonary capillaries, and they then appear to have a special predilection for the long bones, so that widespread involvement of these may occur. A spontaneous fracture may be the first indication of a growth in the kidney. The secondary growths usually closely resemble the primary one, so that a diagnosis of hypernephroma may be made from an examination of the bone lesion. The adrenal shares with the breast, the thyroid, and the prostate this peculiar tendency to implicate the bones in a common ruin.

OTHER KIDNEY TUMORS

Many other varieties of tumor have been reported as occurring in the kidney. These will be found described in textbooks of pathology, but the general design of this book does not warrant a detailed discussion of them here.

Small nodules causing no symptoms may be found at autopsy, *fibromas*, chiefly in the pyramids and papillæ, *adenomas* chiefly in the cortex. True *sarcomas*, round-celled or spindle-celled, probably always arise in the capsule, from which they invade the kidney. *Carcinoma*, adeno-carcinomatous in type, has been reported. It does not show the capsulation characteristic of the hypernephroma.

TUMORS OF THE RENAL PELVIS AND URETER

These tumors are so rare that they merely deserve a passing mention. They closely resemble tumors of the bladder, and may therefore be in their order of frequency:

1. Simple papilloma.
2. Malignant papilloma.
3. Squamous-celled epithelioma.

The renal pelvis is the common site of origin, but in exceptional cases the growth may commence in the ureter. The tumors are usually multiple, and the wall of the pelvis may be covered with masses of finely branched villous processes. These are very friable, and as they are extremely vascular hemorrhage readily occurs. In many instances the condition is associated with renal calculus, and cases have been reported in which a tumor has developed after exploratory incision of the pelvis. Irritation thus appears to play a part of some importance in the etiology.

The tumor tends to grow along the lumen of the ureter, with resulting blocking or hydronephrosis. In the case of the malignant growths particles of tumor tissue may be carried down and implanted on the bladder wall. The second and third varieties are of great malig-

nancy, and secondary growths are set up at an early date not only in neighboring lymphatic glands but in distant organs. The development of squamous-celled carcinoma in a transitional epithelium is to be explained by a metaplasia, the result probably of chronic irritation, which transforms the transitional epithelium of the renal pelvis into a squamous-celled epithelium.

PERIRENAL TUMORS

These extremely rare tumors are of considerable variety, but they all rise from the fibrous or fatty capsule of the kidney. The commonest form is the *lipoma*, which may contain so much fibrous tissue as to deserve the name fibro-lipoma. These tumors may attain an enormous size.

Next in frequency come fibromas and then sarcomas and "mixed tumors," supposed to arise from remnants of the Wolffian body.

Invasion of the kidney practically never occurs, so that renal symptoms are absent. This is a point of great importance in the differential diagnosis, but there are so many conditions with which a perirenal tumor may be mistaken that a correct diagnosis is seldom made.

TUMORS OF THE ADRENAL

Although the adrenal glands have no connection with the urinary tract, it is convenient to consider the subject of adrenal tumors in this place.

The adrenal gland, like the pituitary, consists of two parts which are different in origin, of different physiological function, and present different pathological conditions. The cortex is of mesoblastic origin, yet the tumors which arise from it are of an adenomatous or epitheliomatous character. The medulla is derived from the sympathetic nervous system, and the tumors to which it is liable are nerve cell tumors. The behavior of the two sets of growths is entirely different.

Tumors of Adrenal Cortex.—The common tumor arising from cortical adrenal tissue does not occur in the adrenal but in the kidney, where it has already been studied as the hypernephroma. More rarely tumors are found in the cortex of the gland itself.

At autopsy a small nodule is sometimes discovered, light yellow in color, and seldom larger than a pea in size, a condition which Virchow originally named struma suprarenalis. These masses consist of normal adrenal tissue, and should be regarded as a nodular hyperplasia rather than a neoplasm.

A *diffuse hyperplasia* of the cortex sometimes occurs, as a result of which the adrenal may become as large as the kidney. In the female these tumors are often associated with masculine changes which, in conjunction with a mass in the kidney region, are quite pathognomonic.

Adenoma of the cortex is similar to the nodular form of hyperplasia, but the arrangement of the cells is more atypical and neoplastic. Irregular lumina are frequently seen. As a rule they remain quite small.

Carcinoma, also called adrenal hypernephroma, is the most frequent variety of adrenal tumor. The cases reported as sarcoma are probably of epithelial origin. The tumor usually occurs about middle life. It may attain a large size, and is soft, of a yellow color, and prone to hemorrhage. *Microscopically* the cells may attempt to reproduce the acini of the zona glomerulosa or the columns of the zona fasciculata. In other cases the arrangement is wilder, and no adrenal structure can be recognized. The cells may show a decided perivascular arrangement. Giant cells are sometimes very numerous.

The tumor is very malignant, and *metastases* occur at an early date. There is local extension to the kidney, and the adrenal may completely disappear. The adrenal and renal veins are invaded, as in hypernephroma. Spread takes place both by the blood stream and the lymphatics. The metastases are widespread, but the organs most frequently involved are the liver, lungs, and brain. The opposite adrenal is often affected. The retroperitoneal, mesenteric, and mediastinal glands are enlarged. Contrary to the usual opinion the bones are seldom the seat of metastatic deposits, only in one out of 48 cases collected by Hartmann and Lecene, whereas the liver was involved in 23 cases. Bone metastases are almost always due to growths which arise in the kidney and not in the adrenal.

The *symptoms* are those of an abdominal tumor. Pigmentation may be observed in occasional cases, and well-developed Addison's disease has been reported. Precocious sexual development, obesity, excessive growth of hair, and evidence of other disturbances of the sexual characters are often associated with cortical tumors, never with those of the medulla. A full discussion of this subject will be found in Glynn's paper. It is the male characters alone which develop in children of both sexes, and in women before the menopause.

Tumors of Adrenal Medulla.—Malignant growths of the adrenal medulla form a most interesting group of tumors which is beginning to receive the attention it deserves. They only occur in childhood, and the symptomatology is quite different from that of tumors of the cortex.

Clinical Features.—The disease may be of two types, which may be called, after the observers who first fully described them, the Pepper type and the Hutchison type.

The *Pepper type* was first described in 1901. In Pepper's case the tumor was situated in the right adrenal, and in most of the cases it has been the adrenal on the right side which has been involved. The adrenal may be no larger than a walnut, but the liver may fill the greater part of the abdomen. The enlarged liver is soft and hemorrhagic, and on section is so uniform in appearance that the presence of metastases would never be suspected. Under the microscope the liver substance is entirely replaced by round cells, which used to be mistaken for the cells of a lymphosarcoma. The mesenteric lymph glands are enlarged. The bones of the skull are only occasionally involved. The disease runs a rapid and fatal course of a few weeks.

The *Hutchison type* was described by Robert Hutchison in 1907. The striking feature of the disease is the formation of metastases in the skull and particularly in the region of the orbit, although occasionally other bones, such as the sternum, ribs, and long bones, are involved. Secondary growths are occasionally found in other organs. The first local evidence of disease may be the appearance of an ecchymotic spot round one eye, which the mother usually attributes to a fall. To the physician it may suggest chloroma or scorbutus. At the same time as the appearance of the hemorrhage or a little later proptosis is noticed, and soon a large orbital tumor develops. If the abdomen be now examined a tumor will usually be felt. In a few cases it cannot be detected until a later date.

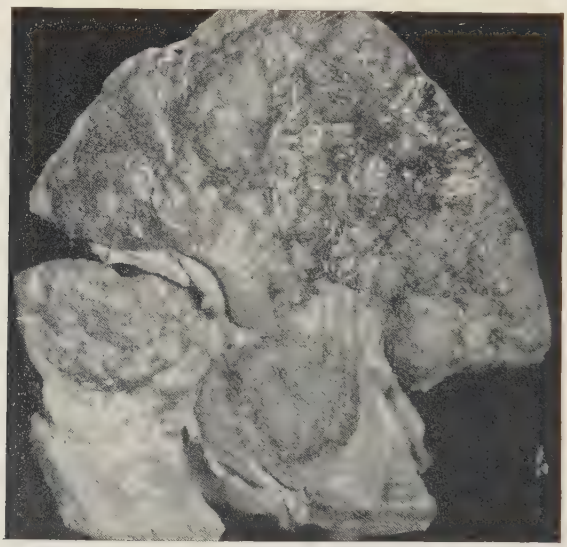

FIG. 153.—Neurocytoma in the liver of a child secondary to a similar tumor in the adrenal medulla.

An interesting study of the mode of spread in 51 cases has been made by Frew. In 47 of these cases there were cranial metastases. In none of the 51 cases was there premature sexual development. Frew points out one extraordinarily interesting fact; when the principal tumor is situated in the right adrenal the right eye or right side of the cranium is commonly involved, when it is in the left adrenal the left side is involved. The mass in the adrenal was larger in the case of right-sided tumors and metastases in neighboring organs were more frequent.

The arrangement of the lymphatics on the two sides is different. On the left the lymphatics draining the adrenal connect with the lumbar glands, some pass down into the groin, others pass upward to the glands around the aorta, to the deep cervical glands, and thence to the skull. The tumor therefore passes down into the pubis and

groin, across to the mesenteric glands, and up through the deep cervical glands and along the carotid artery into the skull. The lungs are never involved, and the liver very seldom.

The lymphatics from the right adrenal do not make connections with the neighboring glands, but pass into the main lymphatic trunk along the vena cava. The upper part of the adrenal is uncovered by peritoneum and comes in contact with the bare area of the liver. Metastases are thus very common in the liver, frequent in the pleura and lungs (owing to extension through the diaphragm), and affect the cervical glands and orbit on the right side. In all the collected cases of right-sided adrenal tumor, the orbital metastases occurred first on the right side.

It is evident, therefore, that extension takes place through the lymph vessels, probably by permeation, and not by the blood stream.

FIG. 154.—Metastatic neuroblastoma in femur and ribs; primary tumor in adrenal medulla.

The disease may be commoner than is usually supposed. Carter, in a recent study of the subject, described three cases which he saw in four months. My own experience is similar, for in the last six months I have encountered three cases, all boys. Curiously enough two of these were Italian children. The eldest was four years, the youngest five months. Two belonged to the Hutchison type, with left-sided tumor and cranial metastases in the orbit and vault of the skull; one was a combined form, with bilateral adrenal tumors, an enormous liver, and cranial metastases in the orbit and base of the skull. In one case of the Hutchison type the tumor did not arise from

the adrenal medulla, but from the sympathetic ganglia along the second, third, and fourth lumbar vertebræ. In this case, however, the adrenal medulla on the left side was replaced by fibrous tissue and numbers of large ganglion cells. The eye was removed because of the extreme proptosis in one case before the abdominal tumor was discovered.

Pathology.—It was Marchand who, in 1891, first suggested that tumors of the adrenal medulla might represent a reproduction of the anlage of the sympathetic nervous system, and the work of J. H. Wright in 1910 has placed this idea on a sure foundation. These tumors, so frequently described as round-cell sarcomas or lympho-

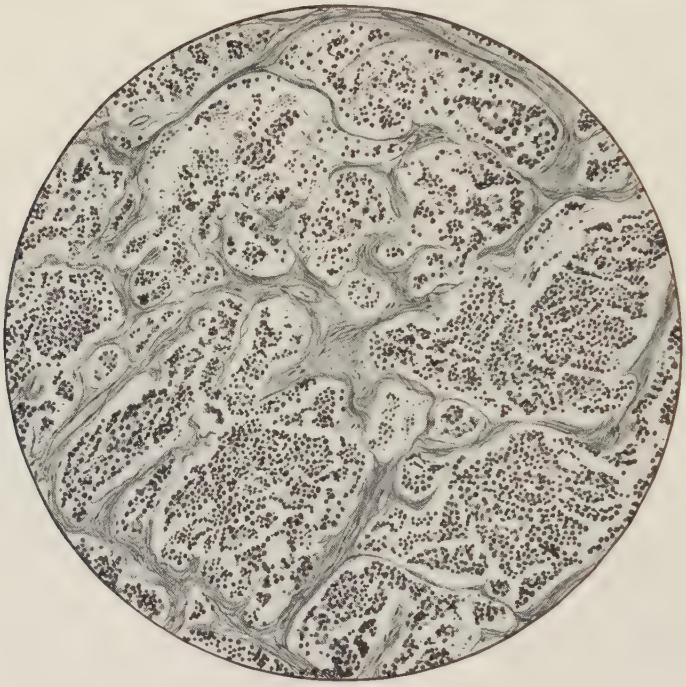

Fig. 155.—Neuroblastoma of the adrenal medulla. The fibrils are arranged in characteristic longitudinal bundles.

sarcomas, are really nerve cell tumors, neurocytomas or neuroblastomas. Indeed it is now regarded as probable that most of the retroperitoneal round-cell sarcomas of infants are of this character, and similar growths have been described in connection with the cervical, thoracic, and peripheral nervous systems. Ewing describes one such tumor which appeared to originate in the femoral sympathetic plexus below Poupart's ligament.

In the *microscopic* picture there are large numbers of round cells like the cells of a sarcoma, fibrils of varying degree of distinctness, and imperfect ganglion cells. The fibrils, which take on a brown

color with van Gieson's stain, are arranged either in longitudinal bundles or as little compact balls round which the cells are grouped to form "rosettes." Such rosettes are seen in the sympathetic anlage from which the adrenal is developed, and they may give rise both to ganglion cells and chromaffine cells. The metastases are composed mainly of round cells, but rosettes and rudimentary ganglion cells have also been described.

CYSTS OF THE KIDNEY

There are three main varieties of cysts of the kidney:

1. Multiple serous cysts.
2. Polycystic kidney.
3. Solitary cyst.

Hydatid cysts and dermoid cysts are pathological curiosities which may be mentioned in passing.

1. **Multiple Serous Cysts.**—These are small cysts found in both kidneys in chronic nephritis, commonly on the surface but occasionally in the substance of the kidney, and due to compression of the renal tubules by fibrous tissue with subsequent dilatation. They are of no surgical interest.

2. **Polycystic Kidney.**—This is a condition the exact nature of which is still shrouded in mystery, as is witnessed by the number of conflicting views which are held on the subject.

The kidney is enlarged and converted into a series of cysts. The condition is almost always bilateral, although usually more advanced on one side than the other. It is somewhat commoner in females than males. The age incidence is peculiar and important. It may develop at any age, but is commonest over forty and during infancy, the intervening years being comparatively exempt. For this reason it has been suggested that the cases occurring in infancy are congenital in origin, whilst those of adult life are acquired.

Even *in utero* the cystic kidneys may attain a remarkable size. In one case which I examined recently the abdominal enlargement was so great that normal delivery was quite impossible, and the fetus had to be eviscerated. The abdominal cavity was almost completely filled by two enormous soft gelatinous masses representing the kidneys, weighing 780 grams; one of these was of the size, shape, and appearance of a huge colloid goiter. The cysts were quite small. Other abnormalities of development were present in the shape of a meningocele and double club foot.

As the exact nature of the condition is unknown, it is not possible to make a definite pronouncement on the subject. It appears probable, however, that all cases are really developmental in origin, due to imperfect union of the units of the renal filter with those of the pelvic portion, but that in the adult cases some additional cause is necessary to bring about the dilatation of the tubules into cysts.

Supporting the developmental theory is the fact that other developmental errors such as cleft palate and other similar malformations are by no means uncommon. Cystic formations in the liver occur with curious frequency, and the two conditions are undoubtedly due to a common cause. Occasionally small cysts are found in the pancreas.

Gross Appearance.—The kidney is enlarged, it may be to three or four times the normal size, and, although preserving its general shape, is studded all over with cysts, so thin-walled that the yellowish or red color of the contents shines through, imparting a variegated hue

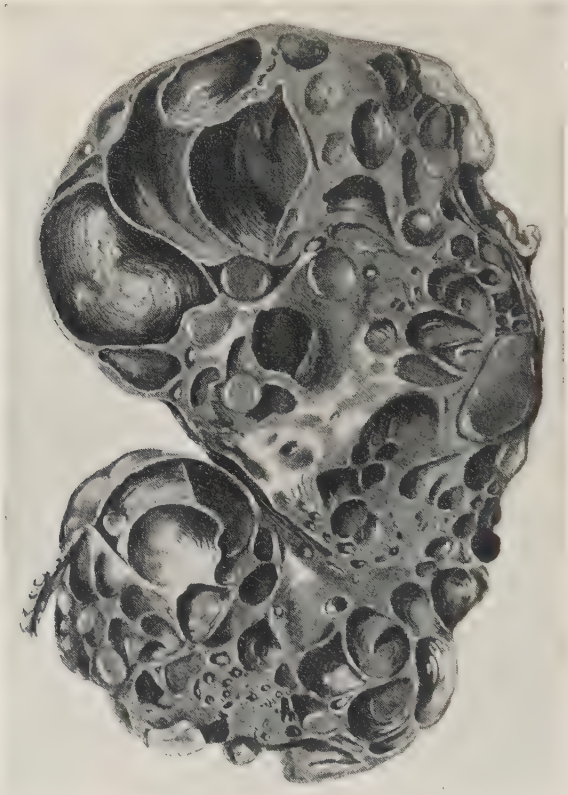

Fig. 156.—Polycystic kidney.

to the tumor. On section the cysts, which vary greatly in size, are found to be scattered throughout the entire kidney. Although occasionally opening into one another they never open into the renal pelvis. The contents vary; they may be thin or thick or viscid, yellow or amber or dark brown from hemorrhage, and although usually non-urinous, they may occasionally contain uric acid and other organic constituents of the urine. In many cases it is so difficult to

find any normal-looking kidney tissue that it seems incredible how a person could remain comparatively well with such an advanced bilateral condition. Localized suppuration is not uncommon.

Microscopically the cysts are lined by epithelium which in the large cysts is flattened, but cubical and even columnar in the smaller ones. The intervening kidney tissue usually shows a marked condition of chronic interstitial nephritis with extensive fibrosis.

FIG. 157.—Solitary cyst of the kidney.

3. **Solitary Cyst.**—A solitary cyst of the kidney may remain small, in which case it will give rise to no symptoms. Occasionally, however, it may attain a great size, in some cases being as large as a child's head. It is a disease of adult life, most of the cases occurring over the age of forty.

The cyst projects from the surface of the kidney, thus producing marked alteration in the shape of the organ. It is usually of a pale color. The contents are serous, and contain albumen and salts, but rarely traces of urea. Hemorrhage into the cyst may occur, and to such a condition the term hemorrhagic cyst has been applied. It is but natural that the larger cysts should often be mistaken for hydronephrosis.

The essential nature of the condition is unknown. It has been suggested by some that it is a congenital malformation, by others that it is a retention cyst due to interstitial nephritis. Needless to say convincing evidence to support either view is completely lacking.

DEVELOPMENTAL ANOMALIES

When we consider the extreme complexity of the kidney, the remarkable manner in which the pelvic portion derived from the

Wolffian duct and the renal filter derived from the nephrogenic mass become fused together, and the very considerable migration upwards from the second sacral vertebra to the region of the second lumbar vertebra before the kidney finds its final abiding place, it is indeed not to be wondered at that abnormalities in development occasionally occur. The number of possible variations is legion, but those of chief surgical importance are the following:—

1. Incomplete development.
2. Misplaced kidney.
3. Fusion of the kidneys.

1. **Incomplete Development.**—There may be any grade of imperfect development, but we may consider three principal types: complete absence, congenital atrophy, and fetal lobulation.

Complete absence of one kidney is due in the great majority of cases to failure of development on the part of the bud from the Wolffian duct which gives rise to the pelvic portion. The ureter, therefore, is also absent. The condition, fortunately, is very rare, occurring once in every 2500 cases. Its surgical importance is evident when the possible removal of the remaining kidney comes to be discussed. Death from anuria would result in the course of a few days. I once saw an asylum patient who was convinced that he had only one kidney, and at the autopsy I could find no trace of the right kidney. There was no scar of any kind.

Congenital atrophy may be of any degree. When at all marked it is accompanied by compensatory hypertrophy of the other kidney. The condition is again of surgical importance, because the small kidney, although otherwise normal, may be unable to carry on by itself should the other kidney be removed. The amount of urine produced is small, and therefore the total urea is diminished, although the percentage may be normal.

Fetal lobulation is a minor error of development, in which the kidney retains the lobulations characteristic of the fetal condition. The surface of the kidney is very irregular. The only importance of the condition lies in the fact that such a kidney shows with all other imperfectly developed kidneys a tendency towards tuberculosis, suppuration, and stone formation.

2. **Misplaced Kidney.**—At any point of its upward progress the kidney may become arrested. As the vascularization of the kidney does not occur until its final resting place has been reached, it follows that when progress ceases too soon, the kidney becomes anchored by blood vessels in its abnormal position. The common positions, in their order of frequency, are at the bifurcation of the aorta, at the sacral promontory, and in the cavity of the pelvis. In the last-named position there are possibilities of trouble should pregnancy supervene. The condition should be suspected when a pelvic mass of uncertain origin interferes with the pregnant uterus.

A misplaced kidney must be carefully differentiated from a movable kidney. The latter has moved from a normal to an abnormal position. The former has never attained to a normal position.

3. **Fusion of the Kidneys.**—Once, it is said, in 1100 cases the nephrogenic masses on either sdie fuse together, and the Wolffian buds growing upwards form separate pelves and ureters for the mass. The condition may be recognized at operation by noticing that the ureter passes down in front of the lower pole of the kidney.

Fusion mostly occurs at the lower poles, although in exceptional cases the upper poles may be united. The condition is called *horse-shoe kidney*. The union may be merely fibrous, or a connecting band of renal tissue may pass across in front of the great vessels. Occasion-

Fig. 158.—Horse-shoe kidney.

ally the fused kidneys may lie one above the other, giving rise to the "S" or *sigmoid kidney*.

Such a kidney is specially liable to be attacked by disease, and in a number of cases it has been possible to resect one side for tuberculosis or septic infection. It has indeed been said that a malignant growth may be confined to one side for a considerable time.

THE URETERS

The ureter shares with the renal pelvis the pathological conditions to which the latter is liable. Suppuration, tuberculosis, stone, and neoplasms inevitably involve the duct of the kidney, and these conditions as they affect the ureter have already been discussed in their respective sections.

Congenital Dilatation of the Ureters.—This very remarkable condition is generally regarded as one of great rarity, and passes entirely unnoticed in the ordinary text-books. It is probable, however, that

Fig. 159.—Congenital dilatation of both ureters due to obstruction in the posterior urethra.

it is commoner than is usually supposed, for I have encountered two examples in the last three years, in the second of which the correct clinical diagnosis was suggested, and Young and his associates at

Baltimore record twelve cases admitted to the Johns Hopkins Hospital during a period of six years.

The condition occurs in male children, although very rarely a case has been described in adult life. The age in my first case was 2½ years, in the second case 12 years. The symptoms are those of gradually increasing urinary obstruction, with dilatation of the bladder and the ureters, an accumulation of residual urine, and failure of renal function. Our first case died of uremic coma; the second, which showed a blood pressure of 230, developed symptoms of pyelonephritis.

The autopsy findings were practically identical in both cases. On opening the abdomen a huge tube was observed running down each side. These at first glance were taken for the ascending and descending colon, but in reality they were merely the enormously dilated ureters. In the first case the ureters were somewhat varicose and sacculated. The kidneys showed a moderate degree of hydronephrosis, but were not greatly enlarged. The bladder was much distended and its wall showed extreme hypertrophy. A valvular obstruction was present in the posterior urethra. An instrument could be readily passed from below upwards, but not from above downwards.

It is now known that in most of these cases the essential pathology is a congenital obstruction of the posterior urethra, valvular in type, and so placed that the concave surface of the valve is directed upward, thus presenting an obstruction to the outflow of urine. The exact nature of the obstructing membrane is still in doubt. In some cases it may be a persistence of the urogenital membrane of the embryo, in others an exaggeration of the normal folds of the posterior urethra associated with the verumontanum, in still others a persistence of fibrous strands which in the fetus may pass from the verumontanum to the roof of the urethra. In a few cases the cause had been a hypertrophy of the verumontanum.

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CHAPTER XXIV

THE LOWER URINARY TRACT

THE BLADDER

The bladder plays the part of a half way house between the upper and lower urinary tracts. It therefore runs a double risk of infection. As an offset to this it must be noted that the healthy bladder is peculiarly resistant to infections. Indeed it may safely be said that, with the exception of tumors, if a pathological condition be found in the bladder the strong probability is that it is not primary in that organ, and that the surgeon must seek elsewhere for the primary focus. This is true for cystitis, for tuberculosis, and for calculi, with the exception of those which occur in old men with prostatic retention. Finally, the bladder resembles the stomach in that it makes its voice heard above that of its neighbors, although usually it is they who are really suffering. Pus in the urine, painful micturition, and frequent micturition are apt to suggest bladder disease. They should not do so, but should rather be taken as an indication of renal disease.

The important diseases of the bladder are cystitis and tuberculosis, which may be regarded as secondary conditions, tumors which are primary, and calculi, which may be primary or secondary.

CYSTITIS

The immunity of the normal bladder to direct infection is quite remarkable. Pyogenic bacteria when introduced in large numbers rapidly disappear without producing any inflammation. There is, therefore, much truth in the remark that there is no such *disease* as cystitis. The real disease must be sought elsewhere, the cystitis being merely a complication which, on account of its obvious nature, forces itself upon the attention of the patient or the surgeon.

These remarks, however, only apply to the healthy bladder. A bladder already weakened by injury or disease is as liable to infection as any other organ. The most important of these predisposing causes are injury and retention.

Injury to the bladder may be done in the course of pelvic operations, especially hysterectomy. Fracture of the pelvis is frequently accompanied by cystitis. But perhaps the most important form of trauma is the presence in the bladder of foreign bodies such as a stone or tumor.

Retention may be due to stricture of the urethra, enlargement of the prostate, carcinoma, or paralysis of the bladder in tabes, injury to the spinal cord, and other nervous conditions. The retained urine undergoes decomposition and produces so much irritation of the bladder

wall in addition to providing an ideal culture medium that infection is certain to occur if bacteria gain access.

Bacteriology.—By far the most common cause of infection is Bacillus coli. Next in frequency come staphylococci and streptococci. Other occasional invaders are the gonococcus, typhoid bacillus, Bacillus proteus, and Bacillus pyocaneus. Infections with the tubercle bacillus are considered separately.

The general rule holds true that coccal infections are acute, bacillary chronic. In colon, typhoid, and gonococcal infections the urine is acid; in staphylococcal, streptococcal and proteus infections the urine is alkaline because these bacteria are ammoniogenic. A peculiar and important feature of the bacteriology of cystitis is that the flora of the bladder may change with a changed reaction of the urine. Thus a colon infection may replace a staphylococcus, or again a proteus may replace a colon infection. During treatment, therefore, both the reaction and the bacteriology of the urine should be carefully watched.

Mode of Infection.—Infection may reach the bladder from the urethra, from the kidney, or by extension from neighboring organs.

Infection from the *urethra* may be due to the passage of dirty instruments, or to the extension of a posterior urethritis.

Infection from the *kidney* is the cause of cystitis in at least 70 per cent of cases. In every case of cystitis, therefore, in which the cause is not quite obvious, the kidney should be suspected. When the renal source of infection is removed the cystitis will as a rule promptly clear up.

Infection from *neighboring organs* is of occasional occurrence. It may accompany pelvic inflammation in women, and also inflammation of the appendix and sigmoid.

Gross Appearance.—In *acute* cystitis the mucous membrane is swollen and intensely red and congested. The normal glistening appearance is lost, hemorrhages are dotted here and there, small ulcers may develop, flakes of muco-pus and shreds of epithelium adhere to the surface, and in the trigone there may be the appearance of tiny clear cysts to which the name of bullous edema has been given. The mucous membrane is freely movable on the underlying muscle.

In chronic cystitis the appearance varies much as it does in chronic cholecystitis. The bladder may show concentric thickening of its wall with corresponding reduction in the size of the cavity. This occurs when the inflammation is marked and there is no retention. The thickening is an inflammatory interstitial one, and is not due to any extent to a hypertrophy of the muscular tissue. If, on the other hand, retention be marked and inflammation only slight, dilatation of the cavity with atrophy of the wall will occur.

The mucous membrane varies in appearance in different parts of the bladder. It has lost its smooth, uniformly pink appearance, and is rough, dull in hue, and mottled with the brown remains of old hemorrhages. In places it may be ulcerated, but elsewhere hypertrophied

so as to form granulomatous masses which project into the lumen. Irregular ridges spoken of as trabeculæ run hither and thither across the bladder, and between these the wall may become pouched into diverticula. The mucous membrane is firmly attached to the muscle, owing to fibrous changes in the submucosa.

Microscopic Appearance.—In the acute stage the changes are for the most part confined to the submucosa, which is much congested and infiltrated with the cells of acute inflammation. The superficial layers of the epithelium may be desquamated, but the deeper layers remain intact, except when ulceration of the mucosa has developed over submucous hemorrhages. The muscle is unaltered.

In the chronic stage all the coats are involved. The characteristic feature is a diffuse fibrosis, most marked in the submucosa. The mucosa is ulcerated in places, but in others it is the seat of an abundant formation of exuberant granulation tissue covered by epithelium, and giving rise to the polypoid excrescences already mentioned. The submucosa is densely fibrosed, and the fibers of the muscular coat are separated by an enormous amount of connective tissue.

Leukoplakia.—In some cases of chronic cystitis the transitional epithelium of the bladder undergoes a metaplasia into cornified epithelium, a condition known as leukoplakia. The change is essentially patchy, and the pale, clean-cut areas are sharply defined from the surrounding mucosa. These lesions, as in the tongue, may form the starting point of an epithelioma.

TUBERCULOSIS OF THE BLADDER

For practical purposes it may be said that tuberculosis of the bladder is never primary. It is always secondary, to tuberculosis of the kidney in the great majority of cases, to tuberculosis of the prostate, seminal vesicles, and epididymis in a few cases, and very rarely to tuberculosis of adjacent organs such as the Fallopian tubes.

In renal cases the disease commences at the ureteric opening, in prostatic cases it begins at the neck of the bladder. Only too often, however, by the time the patient presents himself for treatment the disease has spread to such an extent that the entire trigone is involved. The initial lesion is a tiny, white, translucent tubercle covered by epithelium and situated in the subepithelial connective tissue. Soon, however, ulceration of the overlying epithelium occurs. The *tuberculous ulcer* is characteristically round, with ragged, overhanging edges, and a grey, shaggy floor. Although occasionally covering a considerable area it is seldom deep, and perforation is almost unknown.

The infection is at first a pure tuberculous one, but sooner or later a mixed infection is sure to occur, and the condition becomes one of tuberculous cystitis. Removal of the offending kidney will be followed, in the earlier cases, by recovery of the bladder lesions in the course of a few months. In the later and more advanced cases the duration may be for years or it may be forever.

STONE

The factors concerned in the formation of urinary calculi, together with the different varieties and composition of such calculi, have already been discussed in connection with stone in the kidney. In this section, therefore, only the features peculiar to vesical calculus will be considered.

Stone in the bladder may be primary or secondary. It may commence in the bladder, or, first forming in the kidney, it may pass down the ureter and become a vesical calculus. A primary stone is likely to consist of phosphates or urates. The phosphatic calculus, which is the common variety, is associated with those conditions such as stricture and enlarged prostate which give rise to retention and an alkaline urine. An oxalate stone in the bladder has probably had a renal origin.

The stone may be single or multiple. In the former case it is round or oval. In the latter the stones are cuboidal and frequently faceted.

Spontaneous fracture is a rare and interesting occurrence, one, moreover, which has on occasion been turned to good account by vendors of wonder-working lithia waters. The exact cause of the fracture is not known, but it is probably dependent on an alteration in the internal tension of the stone resulting from a marked change in the specific gravity of the urine.

Reference has already been made to the effect of the presence of a stone upon the bladder. A stone in the bladder is a powerful predisposing cause to cystitis as long as the stone is present. The pressure of the stone may produce a serious degree of ulceration of the bladder wall.

TUMORS OF THE BLADDER

Tumors of the bladder form an interesting and peculiar group, possessing certain characteristics which differentiate them from neoplasms occurring elsewhere. Of these characteristics the most important are (1) the remarkably indefinite line of demarcation which exists between the innocent and the malignant growths, and (2) the tendency displayed by both the innocent and malignant growths to become implanted on parts of the bladder wall.

It may be added in this place that no field for microscopic diagnosis gives less satisfaction to the pathologist than bladder tumors. Indeed it is not too much to say that equally if not more reliable information is to be gained from the cystoscopic study of the naked eye appearance combined with the effect of fulguration on the tumor than from the microscopic examination of a small piece clipped off at random.

The *etiology* of bladder tumors would not be worth discussing until we know something of the etiology of tumors in general, were it not that these growths provide two interesting examples of the relation of chronic irritation to neoplasia. First, it is well known that workers with aniline dyes are peculiarly susceptible to bladder tumors, owing,

it has been supposed, to the irritating effect of the dye excreted in the urine. Second, the leukoplakia occasionally resulting from chronic cystitis may become the site of an epithelioma. On the other hand no relationship has ever been shown to exist between carcinoma and stone in the bladder.

The great majority of tumors of the bladder are epithelial in nature. The nomenclature of these epithelial tumors is confused and voluminous. Perhaps sacrificing completeness for the sake of simplicity, we may speak of bladder tumors as papillomatous, sessile, and infiltrating. The papillomata may be innocent or malignant, the sessile and infiltrating varieties are always carcinomatous.

FIG. 160.—Mucous papilloma of bladder.

Papilloma.—A papilloma of the bladder consists of a number of finger-like processes covered by many layers of epithelial cells. The villi, which usually spring directly from a small circumscribed area of the mucosa, are more fragile and delicate than the fronds of any fern, and when seen with the cystoscope swaying to and fro with every swirl of the fluid in which they float they have the grace and beauty of a sea-anemone. In other cases the villi arise from a well-defined pedicle, but they themselves are then much more short and squat, so that the growth has a raspberry appearance. The mucosa from which the tumor springs is not attached to the muscular cast.

The connective tissue framework of the villi is exceedingly delicate and vascular, consisting largely of capillary loops, that of the pedicle is more fibrous. The whole arrangement may be compared to a tree trunk with spreading branches and delicate twigs. The epithelial cells are columnar in the deeper layers, elongated and tailed in the intermediate ones, and on the surface they resemble those of the normal bladder mucosa. It is to be especially noted that the cells are of uniform size, shape, and staining properties.

The disease is much commoner in men than in women. The innocent varieties usually appear between thirty and fifty, whilst the malignant appear after the age of fifty. The favorite sites are just external to the ureteric openings, at the neck of the bladder, and in the vault. The tumor is usually single, but it is by no means uncommon to find multiple growths.

It is often impossible to distinguish between an innocent and a malignant papilloma either from the gross appearance or by microscopic examination of a small piece of the growth. Only by careful examination of sections from various parts of the tumor can a correct opinion be formed. The old idea that the malignant change always first showed itself as an epithelial invasion of the pedicle is now known to be incorrect. The fatal metamorphosis may begin in one of the villi, leaving the base untouched. In the early stages the important feature is an irregularity in the size, shape, and staining characters of both cells and nuclei. When at a later date epithelial invasion has taken place the diagnosis can be made at a glance.

Are we to say that an innocent tumor may become transformed into a malignant one? Whatever views may be held regarding tumors in other parts of the body, the possibility must be admitted in the case of the bladder. Indeed so frequent is this change that every papilloma of the bladder should be regarded as potentially malignant and treated as such.

Reference has already been made to the curious tendency of both benign and malignant papillomas to set up secondary growths by implantation. This is especially apt to occur after the trauma of an operation, and the surgeon may have the mortification of finding that removal of the original tumor is followed not only by recurrence in the bladder but also in the line of the operation wound.

Carcinoma.—The early stages of the *papillary* form have already been considered. As the disease progresses extensive invasion of the bladder wall occurs, and the cavity may be filled with one or more large, fungating, ulcerated masses.

The *sessile* variety is more squat, diffuse, and infiltrating. It also may give rise to secondary implantation growths.

The *infiltrating* variety forms no projecting mass on the surface, but invades the deeper tissues, giving rise to a typical carcinomatous ulcer with raised thickened edges. The ulcer is single, and the microscopic picture is that of a scirrhous growth with abundant fibrous tissue.

A rare form of carcinoma is the squamous-celled *epithelioma*, which may develop on top of a patch of leukoplakia.

Metastases.—On the whole, cancer of the bladder may be regarded as a fairly localized form of malignant disease. This is particularly true of the papillary form. In the sessile and infiltrating varieties, however, metastases are soon set up. The iliac and lumbar lymphatic glands are the first to be involved. The lungs, the liver, and the spleen are infected through the blood stream. The peculiar liability of the bones to secondary growths from cancer of the prostate is also manifested in the case of cancer of the bladder.

Rare Tumors.—*Sarcoma* is a very rare condition. It is always sessile. It may be round-celled, spindle-celled, or giant-celled.

Myxoma is confined to children. The tumors may be multiple, and are usually pedunculated.

Dermoid cyst may occur in the wall of the bladder, giving rise to that pathological curiosity, pilimiction, or the passage of hair in the urine.

OTHER RARE CONDITIONS

Patent Urachus.—The urachus is a solid cord passing from the apex of the bladder to the umbilicus and representing a portion of the allantois. This may remain patent throughout its entire course, in which case urine will issue from the umbilicus. Or only a portion may remain patent, the remainder becoming obliterated. The latter variety may open internally, it may open externally, or both ends may be closed whilst the intermediate part remains patent.

Ectopia Vesicæ.—Ectopia of the bladder is happily a rare condition, for the lot of the unfortunate sufferer is one of great misery. Owing to a defect of development the anterior wall of the bladder is deficient, the anterior abdominal wall is split with separation of the recti, and the interior of the bladder is exposed. The urine can be seen trickling from the openings of the ureters.

As a therapeutic measure the ureters may be transplanted into the sigmoid, but infection of the kidneys is very liable to occur. As already pointed out, this infection does not pass up in the lumen of the ureter.

Diverticulum of the Bladder.—The etiology of this condition of sacculation is not certain; by some it is thought to be congenital, by others acquired in origin. The condition is very much more common in those past middle life than in the young. In some cases the sac contains muscular fibers, in others the wall consists only of mucous membrane.

PATHOLOGICAL BASIS OF SYMPTOMS OF RENAL DISEASE

At this stage it may be allowable briefly to consider the leading symptoms of a patient suffering from a surgical disease of the kidney, and to determine to which pathological condition they are most likely to be due.

These symptoms are frequent and painful micturition, blood in the urine, and pus in the urine.

Frequent and Painful Micturition.—Either the frequency or the pain may be absent, but usually they are combined. This symptom may point to disease in the urethra, the bladder, or the kidney; in the urethra to a posterior urethritis, gonorrheal in nature; in the bladder to cystitis, tuberculosis or stone; in the kidney to pyelonephritis, tuberculosis, or stone. The bladder is the organ against which suspicion is usually directed. Frequent and painful micturition is, however, rather a renal than a vesical symptom.

Blood in the Urine.—The blood may come from the urethra, the bladder, or the kidney. In the first case the blood comes at the *beginning* of urination and is of a bright red color, in the second it comes in greatest abundance at the *end* of urination and may contain clots, in the third it is *intimately mixed* with the urine, to which it imparts a smoky color.

Urethral hematuria is due to injury or acute inflammation of the urethra or prostate.

Vesical hematuria may be due to a stone in the bladder or to a tumor. In the latter case the hemorrhage is due to the delicate and highly vascular processes being injured by the contraction of the bladder. A tuberculous ulcer in the bladder may give rise to hemorrhage. Rare causes of vesical hematuria are varicose veins and Bilharzia hematobia.

Renal hematuria may be due to acute Bright's disease, chronic congestion of the kidney, paroxysmal hemoglobinuria, and other medical conditions. Surgical causes are rupture of the kidney, stone, and tuberculosis. In addition any inflammatory condition such as pyelitis or pyelonephritis may give rise to bleeding, but the associated pyuria is usually so great as to overshadow and obscure the hematuria.

Of special interest is the condition known as *essential hematuria*, a term intended to indicate that the bleeding, is, as it were, idiopathic and can be traced to no known lesion. The blood is abundant, and readily recognized by the naked eye; indeed the urine may be dark red in color. The bleeding is intermittent, and in the intervals, which may last for weeks or months, no blood can be found. One peculiar feature is that it is strictly unilateral.

Although a cursory examination may reveal no cause for the hematuria, the work of Israel, published more than twenty years ago, showed that most if not all cases have a definite organic basis. In many cases this is a unilateral nephritis, which may be either focal or diffuse. The latter is usually of the interstitial variety. A varicose condition in one of the renal papillæ is sometimes found, due probably to obstruction from interstitial nephritis. Hunner has recently drawn attention to the importance of stricture of the ureter as a cause of essential hematuria. The stricture itself is due to inflammation secondary to some distant focus of infection. The aching or colicky

pains which are not infrequently present may be explained by the presence of a ureteral stricture.

Pus in the Urine.—Any inflammatory condition in the urethra, the bladder, or the kidney may give rise to pyuria.

If the pus comes chiefly at the *beginning* of micturition and the urine is acid, the most probable causes are gonorrheal urethritis and prostatic abscess.

If the pus comes chiefly at the *end* of micturition and the urine is alkaline, the cause is cystitis. The urine may, however, be acid in a pure infection with either Bacillus coli or the tubercle bacillus.

If the pus is *intimately mixed* with the fresh urine and the reaction is acid the pus comes from the kidney, and is due to pyelitis or pyelonephritis, tuberculosis, or stone. The reaction must be tested while the urine is still fresh, else ammonaical decomposition may set in and the reaction may become alkaline.

The Prostate

The prostate gland, although forming an integral part of the lower urinary tract, is a purely sexual organ, and plays no part in the act of urination. Owing to its anatomical situation, however, pathological conditions which in themselves might be regarded as trivial may produce disastrous effects on the entire urinary system.

The important diseases of the prostate are acute and chronic inflammation, enlargement of the prostate, tuberculosis, and cancer.

PROSTATITIS

Inflammation of the prostate may be acute or chronic.

Acute Prostatitis.—This, in the great majority of cases, is due to infection with the gonococcus. An acute gonorrheal urethritis involving the posterior urethra inevitably spreads to the prostate. Three degrees of inflammation may be set up.

Catarrhal inflammation is the most common condition. The ducts are filled with desquamated epithelium and with varying numbers of leucocytes.

Purulent follicular inflammation is a more severe grade of inflammation in which the ducts become blocked with purulent exudate, behind which small abscesses form and discharge into the urethra.

Purulent diffuse inflammation occurs when general invasion of the gland by the gonococcus results in widespread suppuration with destruction of glandular tissue and the formation of abscesses which may occupy the greater part of the prostate. Such an abscess may burst into the urethra, into the rectum, or upon the surface of the perineum. A diffuse cellulitis of the surrounding tissues is a common complication.

Chronic Prostatitis.—This may be a sequel to an acute inflammation which has gradually subsided. More frequently, however, it is gradual and insidious in onset, although due, as in the case of the acute form, to infection with the gonococcus. The gland presents the

changes which would be expected from general principles. The ducts and acini are dilated and filled with catarrhal cells. Areas of round celled infiltration are scattered here and there. Fibrosis and scar formation are present in varying degree in different parts of the gland. The prostate is unduly hard and of varying size, in some cases smaller, in others larger than normal.

It is only to be expected that in such chronic cases the gonococcus will be associated with or replaced by other bacteria. Staphylococci, streptococci, and Bacillus coli are the most frequent secondary invaders.

ENLARGEMENT OF THE PROSTATE

This general non-committal term is used in preference to hypertrophy, hyperplasia, or adenoma because, although various theories as to the nature of the condition have been advanced with great confidence, it cannot be pretended that our knowledge is yet of such a nature as to justify any degree of dogmatism. Such a term as prostatism means nothing and is a mere cloak for ignorance. The prostate may of course be enlarged as the result of inflammation, tuberculosis, or malignant disease. The condition under consideration may be called non-inflammatory, non-malignant, enlargement of the prostate.

Prostatic enlargement is one of the best examples of a disease process with a very well defined age incidence. Only under the rarest circumstances does it occur in early life. It is essentially a disease of the years from 50 to 65.

Some degree of enlargement of the prostate after the age of 50 is the rule rather than the exception. As Sir Benjamin Brodie put it long ago: "When the hair becomes grey and thin, when there is formed a white zone about the cornea, at the same time ordinarily, I dare say invariably, the prostate increases in volume."

Fortunately enlargement of the prostate is by no means synonymous with the development of symptoms. There is no direct relation between the degree of enlargement and the severity of the symptoms. A prostate weighing as much as 40 grams and yet producing no symptoms may be found accidentally at autopsy.

Walker points out the interesting fact that prostatic enlargement is common amongst domestic animals with the onset of old age. This is particularly well seen in the case of the dog. The condition has a wide distribution throughout the animal kingdom.

Before passing to a consideration of the nature of the enlargement and of the effects which it produces a brief reference may be made to the development of the prostate. Without entering into details it may be said that the prostate is developed by the outgrowth of five buds from the posterior urethra. In the early stages of its development it may therefore be regarded as consisting of five lobes, an anterior, two lateral, a middle, and a posterior. Later, however, these become fused together, the boundaries are obliterated, and in the adult no definite subdivision can be made. The so-called middle lobe

of pathology must, then, be differentiated from the middle lobe of embryology.

The passage of the ejaculatory ducts downwards and forwards through the gland divides it into two portions, a posterior lobe and an anterior part made up of the anterior, middle and lateral lobes. The posterior lobe deserves to be thus separately distinguished, for it takes no part in hypertrophy of the prostate, although it may become the seat of carcinoma.

Morbid Anatomy.—The changes are of two main types (1) an overgrowth of the glandular elements, and (2) a diffuse production of fibrous tissue. Depending upon which of these happens to predominate the prostate will be large and soft, or small and hard. One part of the gland may show one condition, another the other.

In most cases the enlargement is due to the formation of one or more nodules, somewhat spongy in appearance, and well delimited from the remainder of the gland. These nodules usually fuse together to form one mass which can readily be shelled out. This mass enlarges at the expense of the rest of the organ, which it compresses to such an extent that it forms for itself a false capsule consisting of fibrous tissue with a little of the old muscular tissue still left. A line of cleavage can readily be set up between the mass and this false capsule. In those cases in which a diffuse fibrosis rather than a glandular hyperplasia dominates the picture such separation is usually impossible.

The enlargement may involve any part of the gland except the posterior lobe. Two lateral lobes and a middle lobe are frequently formed, or the overgrowth may be confined to the middle lobe. This middle lobe is formed by enlargement of the group of glands which lies in the mid-line in the floor of the urethra. It forms a conical mass which projects upwards, dilates the sphincter of the bladder, and may produce, especially when inflammation is superadded, the most extreme degree of retention for reasons presently to be discussed.

The microscopic appearance is one of glandular hyperplasia combined with fibrous and muscular overgrowth. There appears to be a great proliferation and budding of ducts and acini, and the picture at once recalls the somewhat similar appearance seen in thyroid hyperplasia and in chronic mastitis. The epithelium is cylindrical in form, and papillary projections may be so abundant as nearly to fill the glandular spaces. Corpora amylacea may be present, but not in greater abundance than in the normal prostate.

The nature of the condition is still undecided. Many attempts have been made to prove a relationship to gonorrhea, but the evidence is altogether too inconclusive to tarnish the character of respectable old gentlemen. The nodules are usually called adenomata, but the condition is rather one of hyperplasia of preexisting tissue than a neoplastic formation of new glandular tissue. Reference has already been made to the similarity between the microscopic picture in this condition and in chronic mastitis. The two diseases appear to have

much in common. Both affect a sexual gland during the period of its involution. In both there is an irregular epithelial cytoplasia with an accompanying overgrowth of fibrous tissue. It is possible, perhaps probable, that prostatic enlargement is nothing but an abnormality of involution the results of which are particularly noticeable owing to the anatomical position of the gland.

Effects.—Although enlargement of the prostate in itself is a perfectly innocent condition, it may readily be responsible for the death of the patient owing to the secondary changes which it sets up. Every prostatic is threatened by retention followed by infection. Although the bladder symptoms make his life one of extreme misery, yet it is the effect on the kidney which is ultimately responsible for his death.

The prostatic urethra may be much distorted. In addition to being elongated it may be compressed or rendered tortuous. This in itself may produce a certain amount of obstruction.

The *bladder* cannot be completely emptied. In some cases this is due to the ball-valve action of the middle lobe. A more important and constant factor is the elevation of the urethral orifice above the level of the bladder floor owing to the upward growth of the prostate. The effect is the same as if the outlet of a tank were moved from the bottom to a point some distance up the side. Finally, the vesical sphincter may be so dilated by the enlarging mass that it becomes quite incompetent. The effect of all this is to produce a retention overflow. The tank is never empty, and when the urine reaches the level of the outlet it pours over.

As a result of the obstruction the bladder at first becomes hypertrophied, but later dilated. The muscle bands become transformed into thick trabeculæ which give the wall a ribbed appearance. As dilatation proceeds the wall between these trabeculæ becomes pouched into a series of false diverticula. Later the dilatation extends to the ureters and kidneys, producing double hydronephrosis with a corresponding degree of renal insufficiency, as manifested by a lowered phthalein output and by increase in the non-protein nitrogen of the blood. When this inadequacy has reached an advanced stage any sudden removal of the constant high pressure, such as may follow the operation of prostatectomy, is liable to be accompanied by grave symptoms of suppression and uremia. In these cases a blood urea of over 100 mgms. per 100 c.c. must be taken as a contraindication to operation.

Infection is certain to occur sooner or later should the patient have to adopt a catheter life, for the pool of stagnant residual urine is an ideal culture medium awaiting the arrival of even one microorganism from without. The effect of infection is threefold: (1) the production of cystitis, (2) the probable formation of a vesical phosphatic calculus, and (3) the development of a pyelonephritis or pyonephrosis with a degree of renal insufficiency which eventually results in the death of the patient.

TUBERCULOSIS OF THE PROSTATE

Owing to its anatomical situation the prostate may be infected with tuberculosis either from the urinary or from the genital tract. The subject will be considered in greater detail when genital tuberculosis comes up for discussion. The disease process may commence in the prostate instead of spreading from the kidney or the epididymis.

Experimental work has shown that the inital lesion is found just under the epithelium lining one of the ducts. Miliary tubercles are formed which increase in size, giving rise to caseous masses scattered throughout the gland. Although the early lesions are probably on the same side as the infected epididymis, by the time the disease is diagnosed clinically the greater part of the gland is involved, and firm nodular masses can be felt on both sides. Occasionally there is a diffuse tuberculous infiltration without nodule-formation. If caseation is extensive a tuberculous abscess is formed, which may burst either into the urethra or upon the surface. In the latter case a tuberculous fistula will result.

By the time that tuberculosis of the prostate can be diagnosed clinically both seminal vesicles will always be found to be involved.

Tuberculosis of the prostate resembles enlargement of the prostate in that it gives rise to no distinctive symptoms *per se*. The symptoms of the patient are those of tuberculous cystitis, or he may come complaining of an enlarged testicle.

Once tuberculosis has become established in the genito-urinary tract it seldom undergoes spontaneous cure, but when the kidney or the epididymis which is the source of the infection has been removed the disease in the prostate may become quiescent or may actually clear up completely.

CANCER OF THE PROSTATE

Carcinoma of the prostate is by no means the rare disease that until quite recently it was considered to be. It forms from 15 to 20 per cent of all cases of prostatic disease requiring operation (Young).

The idea that cancer occurred as a malignant degeneration of an already hyperplastic gland has had to be abandoned, although hyperplasia may be present as an associated condition in about 50 per cent of the cases. Moreover carcinoma commences in that portion of the gland which is free from the ordinary form of hyperplasia, namely the posterior lobe, although from there it may invade adenomatous masses in the lateral and middle lobes. The usual age incidence is about a decade beyond that of the benign form.

The following description of the pathology by Young is so concise and at the same time so complete that it is given *in extenso*.

"We feel convinced that carcinoma of the prostate does not result as a degeneration of a previously benign adenomatous process; that in about half of the cases it develops where no hypertrophy is present; that in such cases the prostate is little if at all enlarged; that the car-

cinomatous growth follows planes of least resistance; that it is very slow in invading fibrous capsules both of the prostate itself and also of hypertrophied lobes; that the mucosa and submucosa of both urethra and bladder are also very resistant to it; that the most common site for the beginning of cancer is in the posterior subcapsular stratum or lobe, and that from there it may invade the rest of the prostatic glandular tissue, or it may travel upward, escaping from the upper end of the prostate in the region about the ejaculatory ducts, and between the fascia of Denonvilliers posteriorly and the trigone anteriorly; that in its further growth the seminal vesicles and vasa deferentia may not become infiltrated, but in some cases their lumina may become filled with cancer cells and, in the case of the vasa deferentia, these may extend upward for a long distance, the outward walls of the vas remaining apparently intact; that the muscle of the trigone and bladder and also the peritoneum may be invaded from this subtrigonal involvement; and, finally, that the fascia of Denonvilliers, which gives the prostate its most dense capsule posteriorly, is a most effective agent in preventing involvement of the rectum and periprostatic structures." (Modern Urology—Cabot, Vol. ii, p. 659.)

The chief characteristic of the growth is its consistency, which is as hard and dense as that of a scirrhous tumor of the breast. When cut into it imparts the same gritty sensation to the knife as is felt in a breast cancer. The surface is dense, dry, without lobulation, and small yellowish islands composed of carcinomatous cells are seen separated by the more translucent fibrous tissue.

The *microscopic picture* is a varying one, but two main types of growth are encountered, the scirrhous and the adenocarcinomatous. The former is much the more frequent. The scirrhous form is similar to that seen in the breast and elsewhere. Strands and columns of darkly staining cells infiltrate the gland separated by a dense fibrous stroma. In places the stroma may be so abundant that no epithelial elements are visible.

In the adenocarcinomatous variety irregular acini of large cells are scattered here and there, the intervening stroma being infiltrated with wandering epithelial cells. The ducts may be distended with masses of cells presenting a certain resemblance to the papillary masses seen in benign hyperplasia, but they lack the supporting stem of connective tissue characteristic of the latter condition.

It may be asked by what gross features a carcinoma may be differentiated from a benign overgrowth. The chief points of value are (1) the different site of the two conditions, (2) the density of cancer compared with the softness or elasticity of adenoma, (3) the hard thick capsule and gritty sensation on cutting and lack of bulging in the case of cancer, (4) the lack of lobulation and dry surface compared with the nodular and moist surface of the hyperplastic prostate.

The *mode of spread* is of great surgical importance. Commencing as a rule in the posterior lobe the tumor spreads slowly into the lateral lobes, but much more rapidly upwards along the line of the ejaculatory

ducts, emerging at the upper border of the prostate and passing between the bladder and the seminal vesicles, so that it can readily be felt in this position by the palpating finger in the rectum. Invasion of the trigone with ulceration is usually a later occurrence.

Spread to distant parts may occur through the lymph stream or the blood stream. The pelvic and lumbar lymph glands are involved early in the disease, and large metastatic deposits are formed there. Lymphatic spread, either by permeation or embolism, may then involve the thoracic and even the supraclavicular glands, and such organs as the liver, lungs, and pleura may become the seat of secondary growths.

Skeletal metastasis, which occurs in so many cases, must be attributed to blood infection. In this respect the prostate resembles the breast, the thyroid, and the adrenal. Kaufmann gives the figures for skeletal metastases as 70 per cent for carcinoma of the prostate, 37 per cent for carcinoma of the thyroid, and 14 per cent for carcinoma of the breast. Secondary growths in distant bones may occur before it is known that there is any disease of the prostate. When an old man is found to be suffering from a tumor of bone the prostate should always be examined.

RARE CONDITIONS

Sarcoma is a very rare tumor of the prostate. It generally occurs in childhood or early adult life. It forms a soft rapidly growing tumor. It appears probable that most of the tumors which in the past have been regarded as sarcomas of the prostate are in reality anaplastic forms of carcinoma with little or no cell differentiation. The same holds true for sarcomas of the ovary.

Calculus.—Prostatic calculi, forming in the substance of the gland, are generally multiple and millet seed in size. They give rise to few or no symptoms.

The Urethra

The male urethra, which alone will be considered here, is divided into an anterior and a posterior part. The anterior part comprises the penile urethra, the posterior part the membranous and prostatic urethra.

The interior of the urethra does not present a smooth surface, but is indented on all sides by the lacunæ of Morgagni, which are depressions in the mucous membrane, and by the openings of the ducts of the glands of Littré. These glands are situated in the roof and walls and to a lesser extent the floor of the anterior urethra. Lying somewhat deeply in the submucosa they form important harboring places for the gonococcus after it has disappeared from the mucous surface. Normally they secrete mucus. The epithelial lining of the urethra is columnar in type, but as the result of inflammation it may become pavement or even squamous. The latter varieties present a more formidable barrier to the gonococcus than does the

columnar epithelium, and for this reason a second attack is not so intense as the first.

The only common and important pathological condition affecting the urethra is acute inflammation due to the gonococcus, together with the consequences which may result from such inflammation.

GONORRHEAL URETHRITIS

The disease begins as an acute inflammation. By the end of the second day after infection both the lacunæ of Morgagni and the glands of Littré are packed with gonococci and pus cells. By the third day extensive invasion of the mucosa has occurred, the columnar epithelium offering little resistance to the gonococcus and soon becoming desquamated. The pavement epithelium of the fossa navicularis, on the other hand, presents an admirable barrier to the inflammatory process.

In course of time the entire mucosa shows the usual signs of inflammation—congestion and the formation of an inflammatory exudate. The process involves the submucosa, and in severe cases may extend as far as the corpora cavernosa. As a rule the inflammation advances slowly up the urethra until the posterior part is involved. The inflammatory process is much more severe in the prostatic than in the membranous urethra, owing to the great number of glands in the former part. There may be an associated inflammation of the prostate, Cowper's glands, the seminal vesicles, and the epididymis.

The ducts of the glands may become blocked, with the resulting conversion of the glands into pus sacs. In these the gonococcus may linger for considerable periods of time.

The inflammation may clear up in the course of a few weeks. The congestion subsides, the discharge disappears, and the denuded epithelium is replaced, this time however by cells of a pavement type.

On the other hand the inflammation may become chronic. The pus sacs already referred to maintain the inflammation, and the mucosa and submucosa are converted into a granulation tissue, at first cellular but becoming more and more fibrous until at last hard scar tissue is formed. The originally elastic and distensible urethra has now become hard and rigid. The sclerosed tissue constitutes an extensive and irregular scar, which contracts and gives rise to a *stricture* of the tube.

Stricture.—The common *position* for a stricture to develop is in the first inch of the anterior urethra. Although to the surgeon there may appear to be several strictures, or several points at which his instrument is obstructed, the pathologist only finds one scar, on the surface of which may project ridges which serve to catch a sound.

The *effects* of a stricture of the urethra are similar to those produced by an enlarged prostate, and do not therefore require to be considered again in detail. First the bladder and then the kidneys suffer from the constant obstruction. There is one important difference in the two conditions. In prostatic obstruction there is always

a certain amount of residual urine, whereas in obstruction due to a stricture of the urethra the bladder is able to empty itself completely except during occasional brief periods of absolute obstruction caused by congestion at the site of the stricture. Secondary infection is therefore less likely to occur in the latter than in the former condition.

Inflammation and stricture of the urethra may occasionally be due to causes other than gonorrheal infection. Trauma, for instance, either external or instrumental, may produce this condition. Congenital stricture may be due to a valve of mucous membrane, or to thickening of all the coats of the urethra.

Calculus of the urethra is a rare condition, usually due to the arrest of a renal or vesical calculus in its downward passage. I once

FIG. 161.—Urethral calculus which had been present in the penile urethra for thirty years. It consists of two parts.

performed an autopsy on a man who died at the age of 78, and who was aware of the presence of a large stone in the penile urethra for at least 30 years. When he wished to micturate he would push the stone to one side. The bladder was greatly hypertrophied, and both kidneys showed an advanced degree of hydronephrosis.

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CHAPTER XXV

MALE REPRODUCTIVE SYSTEM

The Testicle and Epididymis

The testicle and epididymis may be regarded as one organ. The epididymis is the excretory duct of the testicle. Developmentally, however, they have a separate origin, and it may not be straining analogy too far to compare the male genital gland with the kidney. The kidney develops in two parts, a secreting part and a collecting part; the collecting part, derived from the Wolffian duct, is peculiarly liable to infections either with the tubercle bacillus or with pyogenic organisms, which may reach it by the blood stream or from the bladder, and which may then invade the secreting portion in a secondary manner.

So too the testicle and the epididymis arise separately, the testicle from a mass of fetal tissue lying in front of but distinct from the Wolffian body, whilst the Wolffian duct becomes the duct of the epididymis. The epididymis is the first part of the organ to be attacked by tuberculosis and pyogenic bacteria whether carried by the blood stream or descending from the urethra. This infection may or may not extend to the secreting portion, the testicle.

Enlargement of the testicle may be due, in their order of importance, to inflammation, tuberculosis, syphilis, and neoplasms.

INFLAMMATION OF THE TESTICLE

Inflammation is the commonest disease of the testicle, but it is common in the epididymis and not in the body of the testicle. We may recognize three classes of cases.

1. The inflammation may be practically confined to the epididymis. Gonorrhea is the best example. Tuberculosis at first comes into this category, but later it may spread to the testicle.

2. The inflammation may be confined to the testicle. The orchitis of infections such as mumps, and syphilitic orchitis, belong to this group.

3. The inflammation may involve both testicle and epididymis. Of this traumatic orchitis is an example.

Seeing, therefore, that inflammation tends to be confined to one or other of these parts we may consider under separate headings epididymitis and orchitis.

Inflammation of the epididymis is usually associated with hydrocele, that of the testicle is not, for the dense tunica albuginea by

which the testicle is surrounded serves to prevent inflammation extending to neighboring parts.

Epididymitis

There are two main forms of inflammation of the epididymis, the gonorrheal, and the non-gonorrheal. The gonorrheal infection reaches the epididymis by way of the vas deferens, the non-gonorrheal may follow the same route, or may arrive by the blood stream. Perhaps the last remark is not quite accurate. It is by no means certain that such infections of the epididymis are directly hematogenous. The testicle, it must be remembered, closely resembles the kidney in its development, and may at times assume an excretory function. This serves to explain the not infrequent involvement of the testicle by the organisms of mumps, typhoid, and syphilis. Moreover, the bacteria may fail to find lodgement in the testicle, and may be excreted into the epididymis where they set up a focus of disease. This, probably, is the usual sequence in tuberculosis and may conceivably be the method of infection in gonorrheal epididymitis.

Gonorrheal Epididymitis.—Acute gonorrheal epididymitis is the most frequent complication of gonorrhea, and at the same time the commonest form of testicular inflammation. It is secondary to a posterior urethritis, and occurs in the second and third months of gonorrheal infection.

When we come to consider the route by which the infection travels we are reminded of a similar problem which has already been discussed at some length, the problem of how infection ascends from the bladder to the kidney. The obvious path is via the lumen of the vas deferens. The fact that the inflammation commences in the lower pole, the globus minor, of the epididymis would appear to support this view. But the general principle that infections tend to travel in the same direction as the stream of secretion is a sound one and not lightly to be traversed. The analogy of infections of the kidney suggests that the hematogenous route may be of greater importance than has hitherto been supposed, that the gonococci may be excreted by the testicle into the epididymis, and that there they find so suitable a soil that they set up an inflammation which is confined to that organ.

By whatever route the infection reaches the epididymis the inflammation commences in the lower pole and soon involves the entire organ, although in the milder cases it may be confined to the globus minor. Although it would appear so easy for the infection to spread along the line of the tubules to the testicle that organ remains entirely free. In this respect the analogy with the kidney breaks down. The cellular tissue around the testicle may, however, become involved in the inflammation, so that the testicle may feel enlarged, hard, and tender.

The type of inflammatory reaction is somewhat peculiar and worthy of note. Definite suppuration occurs, with the formation of minute abscesses containing a few drops of pus, but extensive sup-

puration with the formation of large abscesses is rare. The entire organ is involved in a widespread inflammatory edema, and is swollen and tender. In the more acute cases an inflammatory hydrocele is a common accompaniment. The spermatic cord may be involved in the inflammatory process, being tender and indurated, but not to any marked degree.

The disease although acute in onset is equally rapid in decline, provided appropriate treatment is employed, and within a few weeks nothing remains but a few tell-tale scars. Scars, however, are things which cannot always be treated lightly, and the fibrosis may be such as to present an insurmountable obstacle to the passage of spermatozoa. Should the condition be bilateral, permanent sterility will result. Usually, however, the inflammation is confined to one side.

Non-gonorrheal Epididymitis.—Inflammation of the epididymis may occasionally be due to pyogenic organisms other than the gonococcus. This is most likely to occur in conditions such as stricture of the urethra or enlarged prostate where a posterior urethritis is apt to develop. Occasionally, however, it develops without such concomitant conditions. In these cases it is secondary to an infection of the seminal vesicles. The causal organism is usually a staphylococcus, but streptococci and Bacillus coli are occasionally found.

The course of the disease is different from that of the gonorrheal cases. The inflammation commences not in the epididymis but in the seminal vesicle, and from there it spreads slowly down in the walls of the vas deferens. Both the vesicle and the vas become extremely hard and thickened. The speedy resolution of gonorrheal epididymitis is rarely seen in this form. Abscess formation may occur in two places, in the lower pole of the epididymis and in the upper part of the vas at the external abdominal ring. Even after the acute condition has subsided the infection may linger for a long time, so that recurrences are common in contradistinction to their rarity in the gonorrheal variety.

Orchitis

Acute inflammation of the body of the testicle is rare compared with inflammation of the epididymis. At the same time it is not an uncommon affection. There are two main groups of causes:—

1. Trauma.
2. Acute infectious fevers. Of these by far the most important is mumps, then come typhoid fever and small pox, and in a third rare group are many other febrile conditions, too numerous to enumerate.

Traumatic orchitis follows upon a blow on the testicle. The organ rapidly becomes enlarged, but the duration is short, and the condition subsides with equal activity. Atrophy of the testicle may occasionally result.

Metastatic orchitis, due to the formation of a metastatic inflammatory focus, is most typically seen in the case of mumps. The condition develops in about 30 per cent of the cases of this disease. It is usually

unilateral, but may be bilateral. Occasionally it may precede the development of parotitis. It is rarely seen before the age of puberty, and is commonest in young men. The testicle is only moderately enlarged, owing to the firm non-elastic tunica albuginea by which the organ is surrounded. The pain is excruciating, and for the same reason. The epididymis is rarely involved. Suppuration is quite uncommon, resolution is the rule, occurring usually by the end of a week. Atrophy is only too frequent, but the testicle may return to a normal condition.

TUBERCULOSIS OF THE GENITAL TRACT

The site of origin of genital tuberculosis is still a matter for discussion with genito-urinary surgeons. The general opinion is that the disease commences in the epididymis, but Young has recently demonstrated that in many cases, perhaps in most, the primary focus is in the seminal vesicles. From the seminal vesicles the globus minor of the epididymis is generally next attacked, and from the same source the prostate, the urethra, and the bladder may be involved later. The importance of removing the seminal vesicles in any surgical treatment of genital tuberculosis is therefore self-evident.

One point too frequently forgotten must always be kept in mind. Genito-urinary tuberculosis is not an isolated manifestation of the disease. In the great majority of cases tuberculous lesions can be demonstrated in other organs, usually the lungs, and where these cannot be found it may confidently be assumed that they nevertheless exist. From the point of view of treatment, that is of the patient and not merely of the affected organ, this conception is of paramount importance.

In whichever part of the seminal tract the disease may begin the mode of infection must be hematogenous, except in those cases where the bacilli travel from the kidney down to the prostate. As the pathological changes in the testicle are those which specially attract the attention of the surgeon, chief consideration will be given to them.

Morbid Anatomy.—The lower pole of the epididymis is the first part involved. The disease may remain confined to that part, or it may gradually involve the whole of the epididymis, but particulary he upper pole. At first one and then several nodules are formed, so that the whole epididymis becomes considerably enlarged. In the early stages the nodules are very firm and hard, a characteristic which can readily be recognized on palpation. Sooner or later, however, caseation, softening, and liquefaction occur. Tuberculosis in the genital tract seldom displays the natural tendency to healing which is so marked in the lungs. Even if the infection is not advancing it remains ready to spring into activity at the slightest provocation, and the patient once infected has the sword of Damocles continually suspended over his head. When softening occurs the skin of the scrotum may become adherent to the epididymis, with the formation of a tuberculous fistula.

On the other hand softening may not occur, or may be delayed for several years.

Spread to Other Organs.—Tuberculosis does not remain confined to the epididymis. Indeed it is the fact of its early spread to the other parts of the genital tract which makes the determination of the point of onset a matter of so much difficulty. When the patient is first seen by the surgeon, and still more frequently when the parts are examined at autopsy, the epididymis, the vas deferens, the prostate, and the seminal vesicles may all be involved. The path of spread of the infection is a matter of dispute. The obvious route is via the lumen

FIG. 162.—Tuberculosis of the testicle. The epididymis is extensively involved, and the infection is beginning to spread to the body of the testicle.

of the vas, but it is more than possible that it is along the lymphatics in the wall of the vas that the bacilli travel. Finally, it must be remembered that if the blood stream has brought infection to the epididymis or seminal vesicles, the other genital organs may be similary attacked.

The *spermatic cord* is thickened, and hard masses may be felt here and there along its course. Similar nodules are present in the

prostate and seminal vesicles. At a later stage these may caseate and soften.

The *tunica vaginalis* is frequently involved, and its inner surface may be found to be studded with tubercles. A hydrocele is the natural consequence, and may have to be tapped before the outline of the testicle can be made out.

The *testicle* itself may escape for a considerable time, but it will not forever remain inviolate. The first part to be involved is the body of Highmore. The fact that the lymphatics of the testicle concentrate at this point suggest that the path of spread may be lymphatic rather than along the seminal tubules. The disease may remain localized to this part of the testicle, or may spread diffusely throughout the organ.

The condition of *the other epididymis* must be considered in every case. It is a lamentable fact that involvement of the other side is apt to occur no matter what precautions are taken, no matter how radical the operative treatment. Once again the route of infection is a matter of discusson. It is improbable that the bacilli pass along the vas in the direction opposite to the normal stream. More likely the spread is by the lymphatics or by a fresh hematogenous infection.

Finally, the infection may spread to *the urinary tract.* From the prostate one or both kidneys may become involved. A more common occurrence, however, is the downward passage of the bacilli from the kidney to the bladder, with spread to the prostate, vas, and epididymis. About 30 per cent of cases of renal tuberculosis in the male are associated with genital tuberculosis, but the spread is more likely to be downwards than upwards. Still more probable is an independent hematogenous infection of both kidney and epididymis.

SYPHILIS OF THE TESTICLE

Syphilis of the testicle is one of the commonest manifestations of syphilis, but it usually gives rise to no symptoms. It is therefore more frequently seen by the pathologist than by the clinician.

It occurs in two main forms, (1) the gumma, and (2) a diffuse inflammatory infiltration resulting in fibrosis of the organ. Although the former is the more recognized, the latter is infinitely the more common. Both forms are usually confined to the body of the testicle, although occasionally the epididymis is involved in the diffuse variety.

A *gumma* forms a hard mass of varying size, producing enlargement of the testicle. At first it is of a greyish-red color, but later becomes more and more white and fibrous. The caseous center and the presence of occasional giant cells at the periphery may lead to confusion with tuberculosis. Softening is uncommon and the elastic fibers in the walls of the tubules are not destroyed as they are in tuberculosis. Antisyphilitic treatment usually produces a remarkable effect upon the gumma, a point of great importance in differentiating the condition from neoplasm. Although the gumma disappears its place is taken by dense scar tissue.

The *diffuse inflammatory form* is probably of frequent occurrence, although it does not attract the attention of the patient by the production of symptoms. The researches of Warthin have shown that it is one of the commonest manifestations of syphilis. The testicle is not altered in shape, but in the later stages may be markedly atrophic. It is of a characteristic woody hardness, and not only is there an absence of pain and tenderness but the normal testicular sensation is lost. The tunica albuginea is thick and fibrous, and the gland is pervaded with innumerable fine white fibrous bands. These may invade every part of the testicle, or they may be more or less confined to one part. When the normal testicle is cut into the tubules bulge forward in a characteristic manner. The cut surface of the syphilitic testicle remains perfectly flat, because the tubules are bound down by the abundant fibrous tissue. Should the epididymis be involved it is usually the upper pole which shows the change to the most marked extent, and if enlarged in the earlier stages it may form a helmet-like covering to the body of the testicle.

The *microscopic picture* depends entirely upon the stage of the disease. At first the tubules are separated by a diffuse infiltration of lymphocytes and plasma cells, and spirochetes in abundance can be demonstrated by the Levaditi method. A young connective tissue is formed which becomes more and more fibrous, until finally the testicle may be little more than a mass of fibrous tissue. The cells lining the tubules show a marked degree of fatty degeneration, and become desquamated so as to lie in masses within the lumen. Eventually the tubules atrophy and disappear.

It must be borne in mind that the condition known as *fibrosis testis*, although usually the result of syphilitic infection, is by no means so in every case. Other varieties of orchitis may have a similar termination, and even a pronounced arteriosclerosis may produce the same end result. This of course is merely in agreement with what is found elsewhere. A scar in the heart wall may be the result of a syphilitic infection, an acute myocarditis, or sclerosis of the coronary arteries.

TUMORS OF THE TESTICLE

The subject of tumors of the testicle is a confused and bewildering one. On looking through the literature a vast number of different varieties will be found described, several of which appear to masquerade under different names. The result of recent work on these tumors has been to effect a considerable amount of simplification, and to group the multitudinous varieties into a few main classes. Of these classes the most important are:

1. Embryonal tumors.
2. Mixed tumors.
3. Teratomas.

Embryonal Tumors.—This is the largest and most important group. The tumor is soft, rapidly growing, with areas of necrosis and

hemorrhage, and produces extensive destruction of the testicle, which may be represented merely as an outer shell or covering. In the past these tumors have been described as carcinomas or sarcomas, depending upon the type of cell which happened to preponderate. It is probable, however, that they arise neither from the adult differentiated cells lining the tubules nor from the connective cells of the stroma, but that they are true embryonic tumors originating from a segregated blastomere.

The cells are large, spherical, or polyhedral, sometimes arranged in masses or sheets, at other times being scattered more diffusely. The stroma is often very rich in lymphocytes. Although the greater part of the growth may present this structure, one or two portions may present distinct evidence of the embryonal nature of the tumor. In other cases, however, no such evidence may be obtainable.

Mixed Tumors.—The majority of the remaining tumors of the testicle belong to this group, the members of which are responsible for most of the confusion which prevails. Almost any kind of tissue may be found, now one, now another prevailing, so that we may find cartilage, bone, glands, muscle, or nervous tissue. The explanation appears to be that the tumor arises from a cell which has not yet become differentiated for the formation of adult tissues. It is therefore totipotent, that is to say it possesses tridermal potentiality and may give rise to tissue which normally originates from any of the three great embryonic layers. In the testicle there seems to be a marked tendency for one tissue to dominate the others, so that the tumor comes to consist of cartilage, muscle, or glandular tissue, and may readily be mistaken for a chondroma, a myoma, or an adenoma.

Teratomas.—In this small group of rare tumors a more or less successful attempt is made at the creation of a new individual, and definite rudiments of organs may be recognized. Thus skin with sweat glands, bony plates, portions of skull, brain tissue, and groups of ganglion cells may be found.

Reference may be made in this place to the rare formation of a true *chorionepithelioma* in the testicle. This extraordinary occurrence is attributable to the formation of a chorion from the embryonic rudiments, and this in turn gives rise to a tumor which behaves in every respect like a typical chorionepithelioma.

The various testicular tumors vary somewhat in their malignancy, but both the first and second groups usually recur after removal, and give rise to wide-spread metastases. The chorionepithelioma is intensely malignant. Spread by the veins is most common, and metastases are formed in the lungs, liver, brain, and other viscera. In the secondary growths one type of tissue usually predominates, so that the anomalous condition of widespread chondromata or adenomata has frequently been recorded. The spread may be by the lymphatics, and large masses may be formed in the abdominal, mediastinal, and even the cervical lymphatic glands, which may divert attention from the primary growth.

UNDESCENDED TESTICLE

The descent of the testicle is accomplished by so complex a mechanism and the distance traversed is so great that there can be little wonder if a hitch should occasionally occur. The testicle may be arrested at any point in its course from the lumbar region to the scrotum, but the usual positions are:

1. In the neighborhood of the kidney,
2. At the internal abdominal ring,
3. In the inguinal canal, and
4. At the external abdominal ring.

Of these much the commonest position is in the inguinal canal itself.

Many causes have been assigned for the failure in descent, and it is probable that more than one factor may be responsible. Peritoneal adhesions around the testicle, an unduly small external ring, and a failure in the power of the gubernaculum are amongst the many causes which have been suggested.

Effects.—An undescended testicle, especially one situated in the inguinal canal, is in a position of danger. (1) It is liable to attacks of orchitis due to trauma either in the form of a direct blow or from muscular contraction of the abdominal wall. (2) It is more likely to undergo torsion than the normal testicle, and the effects are more severe. (3) Malignant growth is supposed to be more common in the undescended testicle.

The gland itself early undergoes atrophic changes. The sexual cells disappear and the spermatogenetic power declines, so that an undescended testicle is usually sterile. The interstitial cells, on the other hand, often appear to be larger and more abundant than usual, and the virile power is retained. In some cases all the parenchymatous cells disappear and only a mass of fibrous tissue remains.

TORSION OF THE TESTICLE

Torsion may occur either in the fully descended testicle or in the undescended testicle. The latter is the more frequent and the more severe. The usual exciting cause is some sudden muscular effort, but cases have been reported which have occurred during sleep. It is commonest in boys and young men.

The twist may occur in either direction and may be from one to four turns. The vessels below the twist are thrombosed, those above it are normal. The tunica vaginalis contains bloody fluid, and the testicle is extremely congested, hemorrhagic, and almost black in color. If the condition is unrelieved gangrene may supervene. Both from its mode of onset and its clinical symptoms torsion of the testicle is apt to be mistaken for strangulated hernia.

HYDROCELE, HEMATOCELE AND VARICOCELE

Hydrocele

A hydrocele is a sac containing fluid situated within the scrotum. The sac may be the tunica vaginalis, it may form part of the spermatic cord, or it may lie on the surface of the testicle but apart from the tunica vaginalis. Of these varieties the first is by far the commonest.

Hydrocele of the Tunica Vaginalis.—The tunica vaginalis is distended with fluid. This fluid from its composition is evidently inflammatory in nature. The inflammation may be acute and readily recognized, or it may be chronic and of obscure nature. Thus any

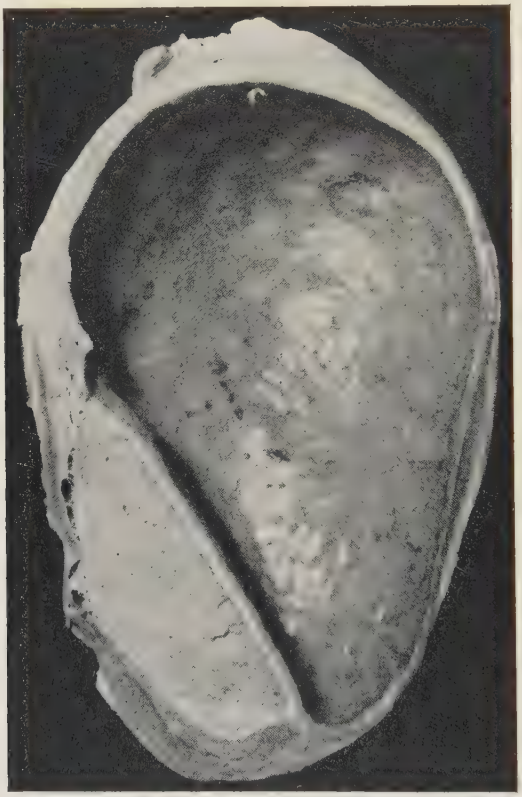

Fig. 163.—Large chronic hydrocele with thick-walled sac. The testicle shows the effects of compression.

inflammation of the testicle or epididymis may spread to the tunica vaginalis and give rise to an acute hydrocele. Inflammation of the epididymis is much more likely to behave thus than is inflammation of the testicle. The two infections most often associated with acute hydrocele are gonorrhea and tuberculosis, both of which involve the epididymis rather than the testicle. It may be that the thick

tunica albuginea serves to prevent the outward spread of infection from the testicle. Chronic hydrocele may represent the after-effect of the acute form, but in the great majority of cases it comes on insidiously, and no satisfactory explanation for it can be assigned.

We may consider the fluid, the sac, and the effects of the hydrocele.

The *fluid* varies, naturally, as the case happens to be acute or chronic. In the acute form it is moderate in amount, seldom exceeding 3 oz., collects rapidly, and is of varying degrees of turbidity, being in some cases frankly purulent. It contains flakes of fibrin and numerous leucocytes. The fluid in the chronic variety may collect so as to produce enormous distension of the scrotum, is clear, thin, and watery, of a yellow or straw color, neutral in reaction, and with a specific gravity of from 1020 to 1025. It contains sodium chloride, carbonates, 6 per cent of albumen, and some fibrinogen, but does not coagulate spontaneously. Occasionally it may present a shimmering appearance due to the presence of cholesterin crystals. In some cases small fibrous bodies may be present, probably owing to the deposition of salts which become covered with fibrin. Endothelial cells, leucocytes, cholesterin crystals, and sometimes spermatozoa make up the microscopic picture.

The *sac* may be thin or thick, depending on the acuteness of the condition. In cases of long standing, and especially in those which have been subjected to repeated tapping, an extraordinary degree of thickening may occur. The wall may become as hard as cartilage, and calcareous plates may be deposited in it. Fibrinous adhesions may cause partial obliteration of the sac, and may divide it into compartments. The hydatid of Morgagni may be considerably elongated, and a causal relationship between this and the recurrence of the hydrocele has often been suggested, but the idea is without adequate foundation, for such enlargement may often be found without any accompanying hydrocele.

The *effect* on the testicle may be nil. When, however, the pressure has been severe and prolonged there may be marked thickening of the surrounding fibrous tissue with flattening or atrophy of the gland. In some cases when the pressure is removed the testicle may return to its original size.

Hydrocele in young people may communicate with the abdominal cavity owing to an unobliterated processus funicularis, or it may pass for a varying distance along the cord owing to partial obliteration of the processus. The former is called *congenital*, the latter *infantile hydrocele*.

Encysted Hydrocele.—Two fairly common conditions are included under this heading, encystic hydrocele of the epididymis and encysted hydrocele of the spermatic cord. They are, however, very different, and it is regrettable that they should be known by the same name.

Encysted hydrocele of the epididymis, better called *spermatocele*, is a condition of dilatation of the spermatic ducts. It forms a small globular swelling at the upper end of the epididymis, frequently situated between that organ and the testicle. The fluid is quite different from that of a hydrocele, bears no traces of an inflammatory origin,

contains hardly any albumen, and is of a peculiar milkiness due to the presence of innumerable spermatozoa. The cyst is usually single, but may be multiple or multilocular.

Encysted hydrocele of the spermatic cord is an entirely different condition. It is merely an unobliterated portion of the processus funicularis lying between the testicle and the internal abdominal ring, which contains a small quantity of clear fluid, and does not communicate with the tunica vaginalis.

Hematocele

A hematocele is a collection of blood in the tunica vaginalis. Other varieties of hematocele have been described to which passing reference will be made. They are of little importance.

The condition is usually associated with a hydrocele, and is due to trauma of some kind. Such trauma may result during the tapping of a hydrocele from mechanical injury to a vein, or the more sudden reduction of the pressure may cause a vein to give way. In other cases a kick or blow is the exciting cause. Occasionally the hematocele may develop without any antecedent trauma. Such cases may be due to the vascularization of an exudate on the surface of the testicle with giving way of one of the new-formed vessels, suggesting the somewhat similar mechanism in pachymeningitis hemorrhagica.

The *fluid* is dark, varying in tone from red to brown, and consists of blood mixed with hydrocele fluid. The center of the tunica vaginalis is occupied by a soft breaking-down clot, but the walls are covered with many layers of fibrin, which later become organized and in some cases calcified. Crystals of hematoidin and cholesterin may be found in the fluid.

Other rare forms of hematocele have been described. A hematocele of the cord is merely an effusion of blood into an encysted hydrocele of the cord, or a diffuse effusion into the cellular tissue. A hematocele of the testis is an extravasation of blood between the testis and the tunica vaginalis.

Varicocele

Varicocele is a condition of varicosity of the pampiniform plexus, the group of 6 or 8 veins which pass up the cord, and fuse at the internal abdominal ring to form the spermatic vein. As in the case of hydrocele it may be secondary or primary.

The *secondary* variety is the result of pressure on the spermatic vein, usually owing to an abdominal tumor, especially a tumor of the kidney. It develops rapidly, and the veins do not empty when the patient lies down. In consequence of its etiology it is principally found in elderly men.

The so-called *primary* form is infinitely commoner. We call it primary because no universally accepted cause has so far been assigned for it, although as usual suggested explanations are remarkable for their number and ingenuity. It occurs principally in young

unmarried men, and is probably associated with chronic venous congestion consequent upon unrelieved sexual stimulation. In at least 90 per cent of cases it is confined to the left side. The left spermatic vein enters the renal vein at right angles, whereas the vein on the right side enters the inferior vena cava at an oblique angle in the direction of the blood flow. The suction, therefore, is less efficient on the left than on the right. A loaded rectum, moreover, may press upon the left vein.

The veins of the plexus become elongated, tortuous, and give to the palpating finger a sensation suggesting a bag of worms. The dilated veins empty when the patient lies down. Thrombosis is a somewhat uncommon complication, and in cases of long standing a phlebolith may form.

The Penis and Scrotum

THE PENIS

Phimosis is a common condition in children. The opening of the prepuce is so small that retraction over the glans is impossible. The condition is congenital, and all degrees may be encountered.

Even in the milder forms there is difficulty in urination, and in the course of time this may lead to serious changes in the bladder and kidneys. The bladder becomes trabeculated, and in some cases dilatation of the ureters and hydronephrosis may develop. Preputial stones may form, sometimes in large numbers, owing to the deposition of smegma, epithelial débris, urinary salts, and cholesterin crystals. These stones are small, soft, and brown in color. Occasionally a stone of considerable size may form. A condition of balanitis is often associated with phimosis.

One of the important relationships of phimosis is cancer of the penis. In over 70 per cent of cases of carcinoma of the penis phimosis is or has been present.

Carcinoma.—This is epitheliomatous in type. It occurs at the usual cancer age, and almost invariably begins either on the glans or on the prepuce. It appear first as a small wart, the nature of which may remain unsuspected for a considerable time. All such warts occurring in elderly men should be regarded with the gravest suspicion, as they are almost certain to prove carcinomatous. Gradually a large fungating cauliflower-like mass is formed, extensive ulceration occurs, and large portions of the organ may be destroyed, with the formation of sinuses communicating with the urethra. The scrotum, testicle, bladder and prostate may become involved. Secondary growths appear first in the inguinal glands, and later in the retroperitoneal groups. Metastases in distant organs occur late in the disease.

Innocent tumors and sarcoma are very rare. So also are tuberculosis and gummatous formation.

Calcareous deposits may form in old people, causing pain and distortion of the organ on erection. These deposits may correspond to the formations of true bone found in some of the lower animals.

THE SCROTUM

Inflammation of the scrotum is due in the great majority of cases to extension of infection from neighboring structures, especially the testicle. Occasionally the condition is a primary one, and in debilitated subjects erysipelas may develop.

Many skin diseases affect the scrotum, but discussion of these would be out of place here.

In tropical countries *elephantiasis* of the scrotum is a common condition. This is due to lymphatic obstruction from blockage of the lymphatics by the Filaria sanguinis hominis. It is the adult worm which produces the symptoms of the disease. The larvæ, the detection of which in the blood stream by night affords the clue to the diagnosis, apparently cause no symptoms.

Syphilis is a common affection of the scrotum. A primary chancre may occasionally occur in this situation. In the secondary stage moist patches and condylomata are frequent. Later in the disease a gumma may develop. Much more usual, however, is involvement of the scrotum by an ulcerating gumma of the testicle.

Carcinoma of the scrotum is so similar to carcinoma of the penis in its general characteristics that it does not call for special description. It is of course epitheliomatous in type. A point of great etiological interest is its relation to the irritation produced by the continual presence of soot in the folds of the skin, so that it has been called chimney sweep's cancer. It also occurs in workers with coal tar and with paraffin. The condition is very much more common in England than in America.

Reference for Further Study

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CHAPTER XXVI

FEMALE REPRODUCTIVE SYSTEM

THE UTERUS

Anatomy.—The uterus is a pear-shaped organ consisting of two parts, the body and the cervix. These present certain differences in structure, they differ markedly in function, and they react to disease in very different ways.

The uterus consists of three coats, a serous covering of peritoneum, a muscular coat, and a lining of mucous membrane. It is chiefly in respect to the mucosa that the body differs from the cervix in structure.

The *middle coat* is made up of bundles of plain muscle fibers separated by fibrous tissue. The proportion of muscular to fibrous tissue varies at different age periods. During the period of functional activity the proportion of muscle to fibrous tissue is 3 to 2. The importance of an abundance of muscle fibers is realized when it is recalled that the muscle is essential not only during periods of pregnancy, but for the control of menstrual bleeding. If for any reason the proportion of fibrous tissue becomes greater the control of bleeding will become correspondingly less. Before puberty and after the menopause the proportion of muscular to fibrous tissue is 2 to 3.

Three layers of muscle are described, an outer, a middle, and an inner, but these are difficult to make out, and are of no importance from the pathological standpoint. In the cervix the muscle fibers are not arranged in bundles, but are diffusely interwoven with the fibrous tissue.

The *endometrium* or inner coat is the mucous membrane of the uterus. It presents certain peculiarities of structure which demand attention, for unless one be familiar with them it is impossible to interpret aright the pictures seen in pathological states.

The endometrium of the body is smooth and shiny, and about 2 mm. in thickness, although after the menopause it naturally undergoes atrophy. In the cervix it presents a series of transverse folds terminated by two ridges, one on the anterior, the other on the posterior wall. The lining is of tall, columnar, ciliated epithelial cells. In pathological specimens, however, the cilia can seldom be seen. At the external os the columnar epithelium gives place abruptly to the stratified squamous epithelium covering the vaginal portion of the cervix.

The remainder of the mucous membrane is composed of an abundant stroma, into which long tubular glands dip down from the surface. Many of these glands reach the muscular layer and may even

penetrate into it for a short distance, a fact to be kept in mind in studying a section for evidence of carcinoma. There is no submucous coat in the uterus. This, together with the fact that the glands penetrate the muscularis, makes it impossible to strip off the mucosa as can be done in other organs. It has to be actually scraped away.

In the cervix the surface epithelium is taller, the glands are more numerous and complex, and they produce an abundant mucoid secretion which, if the opening become plugged, produces distension of the gland with the formation of Naboth's follicles.

The *stroma* merits special attention, as it differs from that of any other mucous membrane, and its peculiar character leads to considerable difficulty in recognizing certain pathological conditions. It consists of an open network of collagen fibers throughout which are scattered numerous cells. These are of two varieties. The more numerous, which may be called stroma cells, are bluntly fusiform in shape, with a large nucleus and scanty cytoplasm. The others are small round cells resembling lymphocytes, but probably are embryonic connective tissue cells. It will be realized that in such a cellular structure it will be difficult to be certain whether or not inflammatory changes are present, and to the uninitiated the appearance may even be suggestive of sarcomatous formation. The open nature of the stroma is designed to allow for the edema and the expansion of the glands characteristic of menstruation. As the cervix takes no part in menstruation such an arrangement is unnecessary, and the stroma, which is dense and fibrous, blends with the general fibro-muscular tissue of the wall.

Changes Accompanying Menstruation.—It is impossible to leave the subject of the structure of the endometrium without a reference to the changes which it undergoes during menstruation. Until the significance of these changes was first demonstrated by Hitschmann and Adler many a histological picture was regarded as pathological which we now know to be merely physiological. It is a profound mistake to imagine that the only changes in the mucosa are those which take place during the actual menstrual period. Throughout the entire menstrual cycle of 28 days the endometrium is being played upon by influences from the ovaries, so that it is never in a state of passivity and rest.

The menstrual cycle may be divided into four phases: (1) the premenstrual phase; (2) the menstrual phase; (3) the post-menstrual phase; and (4) the interval.

The *premenstrual phase,* which commences about a week before the onset of menstruation, is one of great activity, and the changes recall to some extent those of the thyroid in Graves' disease. The cells lining the gland change from a low cubical to a high columnar form, and the presence of mitotic figures may indicate the activity of the proliferation process. Feathery projections jut into the lumen, giving the gland a fern-like or corkscrew appearance. In any given section the number of glands appears to be greatly increased. Active

secretion of mucus commences. The stroma becomes swollen, and may be divided into a superficial compact and a deep spongy portion. The superficial part comes to resemble the decidua, owing to the transformation of the stroma cells into cells of an epithelioid character. The blood vessels are greatly distended.

It will be at once apparent that these are the very changes which formerly were recognized as so-called glandular endometritis, a condition which used to be considered one of the commonest in gynecological practice, but which is now known to be much less frequent.

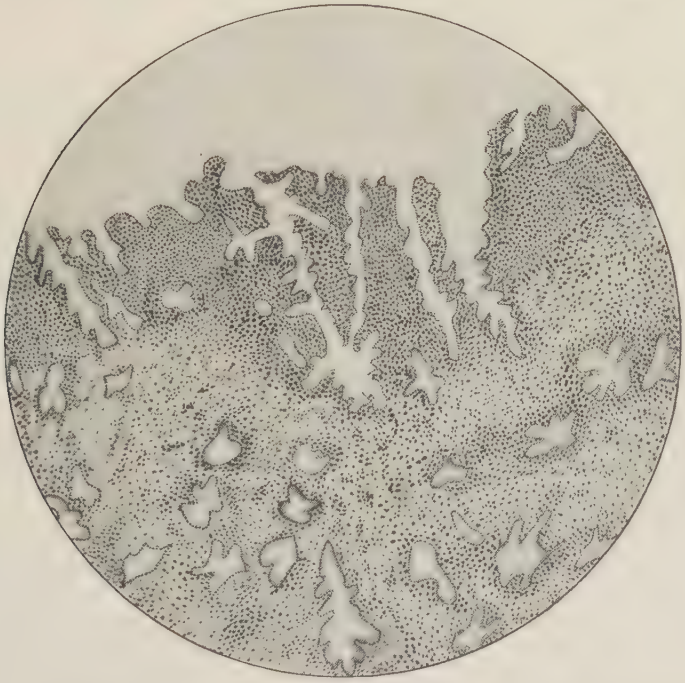

Fig. 164.—Premenstrual endometrium. The fern-like character of the glands is well shown.

In offering an opinion on the nature of a uterine scraping it is therefore essential to know at what phase of the menstrual cycle the specimen was taken.

The remaining phases of the cycle will be merely indicated, as they are not so essential for our present purpose.

The *menstrual phase* is one of exudation. The distended vessels give way, blood is poured out, breaks occur here and there in the lining epithelium, the glands pour forth their mucus, and the flow is established.

The *post-menstrual phase* is one of involution. The entire endometrium shrinks, the glands lose their corkscrew appearance, become simple and straight, cease to secrete mucus, and the cells revert from

the columnar to the cubical type. The stroma cells return to their usual size.

The *interval phase* is not one of quiescence but of repair. Mitosis commences, the glandular epithelium becomes replaced and begins to secrete, the surface lining is repaired, and in time all is ready again for the onset of the premenstrual period.

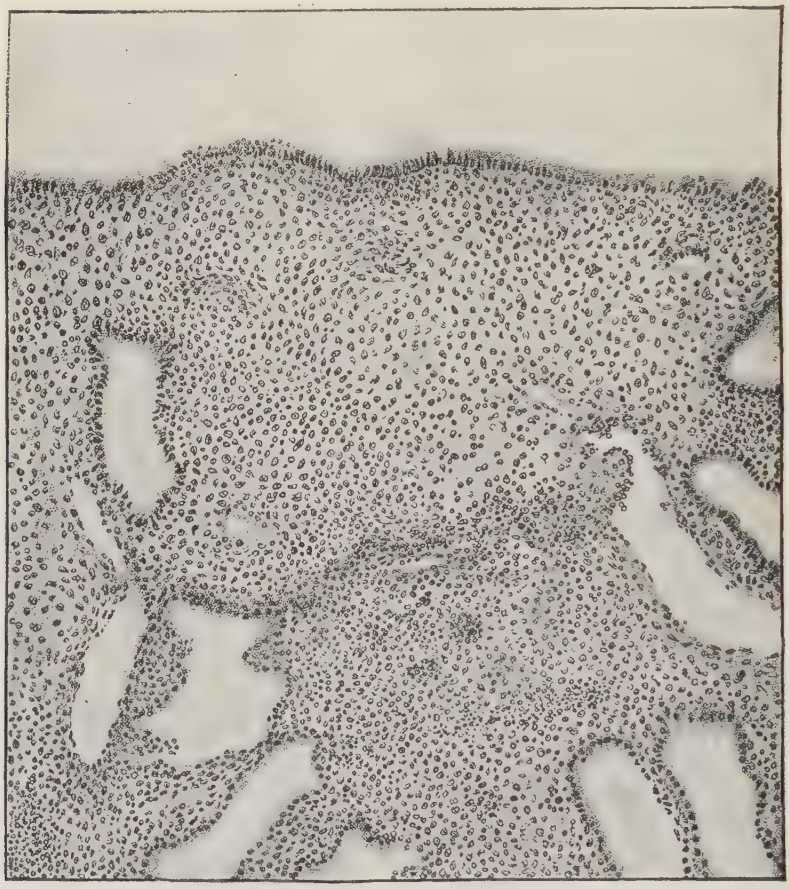

FIG. 165.—Postmenstrual endometrium. (Graves.)

INFLAMMATION OF THE UTERUS

Inflammation of the uterus may effect the endometrium (endometritis) the uterine muscle (metritis), the peritoneal covering (perimetritis), or the neighboring cellular tissue (parametritis). Of these, only the first two will be considered in this place. For a discussion of the other conditions works on gynecology must be consulted.

ENDOMETRITIS

Acute Endometritis.—This may occur in the pregnant or the nonpregnant uterus. The former, known as puerperal sepsis, is by far the

more important and common, and will therefore be described in detail. The chief cause of inflammation in the non-pregnant uterus is the gonococcus. Other conditions which may give rise to it are a necrotic submucous fibroid, an ulcerating carcinoma, the passage of dirty instruments, etc.

Puerperal Endometritis.—The puerperal uterus readily lends itself to infection. When bacteria are introduced into the healthy non-pregnant uterus they are speedily disposed of. In the puerperal uterus, however, there is a large raw surface, and, still more important, there are fragments of tissue deprived of their blood supply and waiting, as it were, for infection. This infection may be by saprophytic

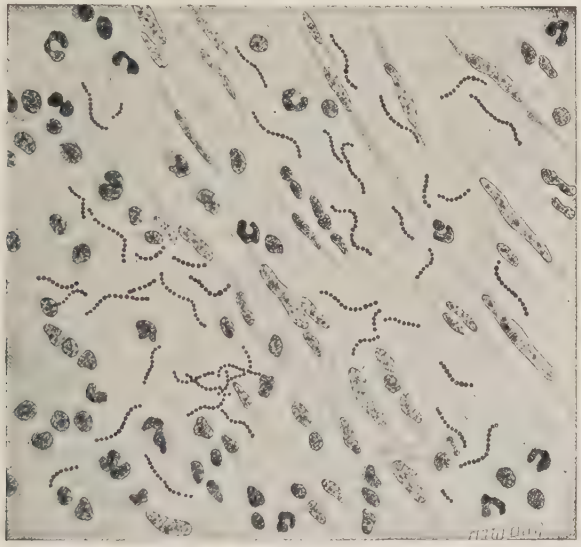

FIG. 166.—Puerperal metritis, showing streptococci in the tissues. (De Lee.)

organisms, of which Bacillus proteus is an example, in which case a condition of sapremia results. The infection is local, but the poisons produced in the decomposing mass are absorbed and give rise to poisoning of varying degrees of intensity. When the local nidus is removed, cure results. If, on the other hand, a virulent pathogenic organism such as the streptococcus hemolyticus is the invader, the infection penetrates further, invades the blood and lymph stream, and sets up a condition of septicemia, and it may be of pyemia.

The local condition is similar in the two cases, but with certain differences. The uterus is soft, flabby, and enlarged. We may note here that infection invariably interferes with involution, and is the most important cause of subinvolution, a subject which will have to be considered presently. The cavity is lined with ragged, greenish-black, decomposing tissue which may or may not have a putrid odor. Under

this layer of necrotic tissue, fibrin, and bacteria there is a protective zone of leucocytes. In cases of sapremia this zone is wide and sufficient to prevent invasion of the deeper tissues, unless it be broken down by injudicious and violent curettage. Deeper still the muscular tissue is edematous but free from bacteria. In streptococcal septicemia, on the other hand, the protective zone is thin and poorly formed, and the organisms can be seen invading the deeper muscular layers. It is essentially a spreading condition.

The extension may take many forms. The invading bacteria may penetrate the muscular wall, infect the serous coat, and set up a peritonitis, at first local, but soon becoming general. Or the broad ligament and neighboring tissue may become infiltrated with the formation of large abscesses. Or the infection may pass along the Fallopian tubes and thus reach the peritoneal cavity with disastrous results. Finally distant parts may become involved by infection through the lymphatics or the blood stream. The veins are represented by great gaping channels filled with septic thrombi, which are at first firm, but soon become converted into foul necrotic debris similar to that lining the cavity, or into actual pus. This material is swept into the blood stream, and forms pyemic abscesses throughout the body, in the lungs, kidneys, joints, etc. The valves of the heart are frequently infected, and an ulcerative endocarditis adds to the gravity of the picture. Such is the course of a septic endometritis in its most terrible form.

Chronic Endometritis.—As has already been indicated, our views regarding chronic endometritis have had to be profoundly modified on account of recent advances in knowledge of the normal physiological changes in the endometrium which accompany the menstrual cycle.

Etiology.—Endometritis is an inflammatory condition, and is therefore due to bacterial infection. In some cases this infection can be definitely determined. It may be due to the gonococcus, to retained portions of placenta especially after an abortion, to the introduction of sepsis from without. Here the infection is more or less subacute at the commencement, later becoming chronic. In other cases the endometritis occurs as a complication of some preexisting pathological condition, such as uterine displacement, prolapse, or the presence of a submucous fibroid. In the majority of cases, however, it is impossible to lay the finger on any definite infection. These cases may be infected from the blood stream. With our present knowledge it is useless to theorize.

Morbid Histology.—The endometrium may behave in two very different ways to a chronic infection, and in consequence two varieties of chronic endometritis are described, the atrophic and the hypertrophic.

In the *atrophic form* the endometrium is much thinner than normal. The glands are few, atrophic, and many have lost their lining epithelium. The stroma is remarkably dense and fibrous, the blood vessels

are thick-walled, and there are numerous plasma cells—a sure sign of chronic inflammation.

It must be borne in mind that a very similar condition of the endometrium is found after the menopause. This is sometimes wrongly named atrophic endometritis, whereas it ought to be called a post-climacteric atrophy. No opinion regarding pathological conditions of the endometrium is of any value, therefore, unless all the facts of the case be known.

In the *hypertrophic form* the endometrium is thickened, and in places it may be raised into polypoid masses. In advanced cases the entire mucosa may have a markedly nodular appearance. The glands are very numerous, dip down into the muscularis to an abnormal distance, and present the active crenated appearance characteristic of the premenstrual period. Many of the lining cells are distended with mucus so as to form goblet cells. Some of the glands may be dilated into large cysts. The stroma is very dense, and is packed with young fibroblasts. Plasma cells are present in large numbers. The blood vessels are very thick-walled.

The picture bears a superficial resemblance to that seen in the premenstrual phase, with which it used to be confused. In addition, however, there are very distinct evidences of inflammation—the dense stroma, the numerous fibroblasts, the plasma cells, the thickened blood vessels. Unless these are present a diagnosis of chronic endometritis is not justifiable.

What is the explanation of the similarity in the two pictures? It is simply that in all probability the hypertrophic form of chronic endometritis is merely a continuance of the premenstrual phase. The most important cause of subinvolution, whether after the major changes of pregnancy or the minor changes of menstruation, is bacterial infection. The endometrium fails to undergo complete involution, and in addition there are the characteristic evidences of chronic inflammation.

Cervical Endometritis: Cervical Erosion.—We have already seen that the cervical endometrium, which plays no part in menstruation, differs in some important particulars from that of the body. It also behaves differently in response to chronic irritation.

Although the term cervical erosion is in everyday use, the condition is in no sense a true erosion, for no raw surface is produced. It is instead a condition of overgrowth of the endometrium of the cervical canal, which displays a tendency to extend its normal limits on to the vaginal portion of the cervix. As the columnar epithelium of the canal has none of the opacity of the dense stratified epithelium of the vagina, the affected area of the vaginal part of the cervix has a red and eroded appearance.

The external os appears red and patulous, and the mucosa is swollen. The line of division between the cervical canal and that part of the cervix covered with stratified vaginal epithelium is no longer sharply defined, and a red patch may be seen on the surface

of the vaginal portion. In some cases the small bluish swellings called Naboth's ovules are very evident.

The commonest causes of erosion are laceration of the cervix in childbirth and gonorrheal infection of the cervix.

In the former case if the tear be a superficial one it is covered by the vaginal epithelium and no harm is done. If, however, it is deep, there is a tendency for the lips of the cervix to become everted, so that the bright red mucosa of the cervical canal becomes exposed to view. Infection is superadded, and the resulting fibrosis still further increases the eversion. At the same time there is a tendency for the cylindrical epithelium to extend on to the vaginal aspect of the cervix and replace the normal stratified epithelium. Owing partly to the infection, partly to the irritation from exposure, the epithelium of the canal, both on the surface and in the glands, proliferates, so that the surface epithelium becomes thickened and the deeper parts present a glandular appearance.

A somewhat similar condition may result from gonorrheal infection. The cervix is thickened and edematous, and once more the mucosa of the cervical canal begins to protrude through the external os. Glandular proliferation and replacement of the stratified by the columnar epithelium proceeds as before.

Microscopic Appearance.—The endometrium is seen to be packed with small rounded cells, particularly in the subepithelial tissue and around the glands. The glands themselves are stimulated to activity, proliferate, secrete an abundant supply of mucus, and become distended. The surface may be covered with papillary projections, each covered by a single layer of columnar epithelium. After a time the squamous epithelium may once more grow over the red patch, or it may be that the columnar becomes converted into squamous epithelium. This process is known as "healing" of the erosion. This new thick epithelium tends to close the mouths of the ducts of the glands, and as at the same time the stroma becomes more and more fibrous and tends to block the ducts, the glands become dilated into Naboth's follicles, which may attain the size of a pea or even larger. The final result of the "healing" is a thick white patch or cervical leukoplakia.

CHRONIC METRITIS: FIBROSIS OF THE UTERUS

It happens not infrequently that a patient between the ages of 40 and 50 suffers from such intractable bleeding at the menstrual periods as to give rise to a strong suspicion of carcinoma or submucous fibroid, and yet when the uterus is examined no trace of a tumor can be discovered. Such cases are usually examples of the condition to which the names chronic metritis and fibrosis of the uterus are given, but for which no entirely appropriate name has yet been found. It is true that chronic inflammation of the muscular coat of the uterus is the most important etiological factor, but the actual condition is

the result rather than the manifestation of the inflammation. It is no more a chronic metritis than a thickened pleura is a chronic pleurisy.

Morbid Anatomy.—The wall of the uterus is invariably thickened, usually to about double the normal size, so that it measures about 1 inch in diameter. The proportion of fibrous to muscular tissue is greatly increased, indeed the greater part of the uterine wall may be fibrous in character, so that it becomes very dense and hard. The walls of the blood vessels are much thickened, and their gaping mouths are a striking feature of the cut surface.

The vascular changes merit more detailed description. During normal involution the fibrous and elastic layers of the arteries become swollen and converted into a hyaline mass. The lumen of the vessel is frequently occluded by a thrombus. In course of time fibroblasts and muscle cells invade this mass and form the wall of a new and smaller vessel inside of the old one, a new lumen is formed, and a new lining of endothelium appears. When involution is complete no trace of the old elastic tissue is left, although some of the fibrous tissue usually remains. When involution is interfered with owing to infection this process of obliteration of the fibrous and elastic tissue is correspondingly incomplete, and in sections stained by Weigert's elastic tissue stain large amounts of elastic tissue may be seen outside the wall of the new vessels. This elastic tissue seriously interferes with the contraction of the uterine muscle which is so important a factor in the control of menstrual bleeding. The endometrium may be considerably thickened, but this is not invariably the case. When it is, it probably contributes to the menorrhagia.

The condition is essentially one of subinvolution in which the excess of fibrous and elastic tissue interferes with the muscular contractions. The subinvolution is due probably to infection in the great majority of cases, although all direct traces of that infection may have vanished. At least 85 per cent of the cases occur in women who have borne children.

Occasionally a nullipara may exhibit symptoms of chronic metritis about the time of the menopause. In such cases the condition found is somewhat different. There is a real *hypertrophy* affecting all the elements of the uterine wall, the endometrium, the muscle, and the fibrous tissue. As the uterus has never had the opportunity to undergo involution none of the changes of involution or subinvolution are found. The vessels are normal, and the general appearance that of the virgin uterus.

Finally, rare cases of intractable hemorrhage may occur at or soon after puberty for which no explanation can be offered. In one case, a girl of 18 years, the patient nearly died from several tremendous hemorrhages, but when finally, as a last resort, the uterus was removed we could find no cause for the hemorrhage. In such cases it may be that we should look to the ovaries for an explanation.

FIBROID TUMORS OF THE UTERUS

The commonest tumor in the body is the myoma, fibromyoma, or fibroid tumor of the uterus. Of all woman between the periods of puberty and the menopause 1 in 5 have fibroids of the uterus, and in the black races the proportion is said to be as high as 1 in 2 or even 1 in 1.

The age incidence is very definite. These tumors are almost entirely confined to the period of reproductive activity. Their exact cause, like that of all other real tumors, is of course unknown, but the relation of the internal secretion of the ovaries, on which the reproductive activity of the uterus is entirely dependent, must be taken into account. A large corpus luteum in the ovary is not uncommon in cases of large rapidly growing submucous fibroids.

Morbid Anatomy.—A fibroid of the uterus is a true myoma, the type cell is a plain muscle cell, but the proportion of fibrous tissue is

FIG. 167.—Myoma of uterus. The muscle cells are grouped into very definite bundles.

often so great that it may with justice be called a fibromyoma. The tumor originates in the uterine wall, usually in the body; in 8 per cent of cases in the cervix. It is rarely single, and often large numbers are present.

The *microscopic appearance* is one of interlacing bundles of plain muscle fibers, some cut longitudinally, some transversely, separated by

a varying amount of fibrous tissue. The small tumors consist almost entirely of muscle fibers, but the larger and older varieties may be largely composed of fibrous tissue. As a rule the blood vessels are few and thin-walled. The readiest means of distinguishing the muscular from the fibrous tissue is by means of Van Gieson's stain with which the muscle cells are colored yellow, the collagen fibrils pink. Of course if fibroblasts are numerous they also will take on the yellow stain. The nuclei of the muscle cells, however, are shorter, plumper, and cigar-shaped, whereas those of the fibrous tissue cells are more slender, curved, and spindle-shaped.

The *gross appearance* of fibroids is very variable, depending largely upon the various degenerations to which they are liable. In an uncomplicated case the tumor is hard, of a glistening white color, and presents an appearance of numerous whorls not unlike that of the surface of a ball of worsted. The more fibrous tissue it contains the more white and glistening it is. Subserous fibroids are the most fibrous, submucous the most muscular. The hard white tumor is sharply demarcated from the surrounding softer and more reddish-brown muscle, and a very definite capsule of compressed muscle tissue is formed from which the tumor may as a rule be readily shelled out. The capsule is highly vascular and supplies the tumor with blood. The larger the tumor, the further will its center be from the blood supply and the more liable to degeneration.

As the tumor continues to grow three things may happen. It may remain within the wall of the uterus, in which case it is called an interstitial fibroid. All fibroids are interstitial at the commencement. Or it may grow outwards, escape from its capsule, and be covered only by a layer of peritoneum. This is a subperitoneal fibroid. Finally it may grow inwards into the cavity of the uterus, again escape from the capsule, and be covered only by the endometrium. This is the submucous variety.

The *interstitial fibroid* is usually small, but it may cause considerable enlargement of the uterus. Not only may there be distortion due to the presence of the tumor, but there is often an accompanying hypertrophy of the uterine muscle. Not infrequently one tumor commences in the anterior and another in the posterior wall, and as they grow synchronously they produce a dumb bell appearance with the body of the uterus taking the place of the handle. Marked displacement of the uterus in the pelvis is inevitable when the tumors attain to any size. The interstitial fibroid, like the subperitoneal but unlike the submucous variety, interferes neither with menstruation nor conception. Owing, however, to the general turgescence of the uterus which precedes menstruation it may cause stretching of the urethra so that when a woman of middle age complains of retention of urine for a few days before the onset of menstruation a fibroid of the uterus should be suspected. These tumors seldom become calcified or cystic, owing to their fairly efficient blood supply, but they are liable to the red degeneration of pregnancy.

The *subperitoneal fibroid* commences as the interstitial variety and later becomes subserous by being extruded through its capsule. These tumors are usually multiple and may attain an enormous size. They may be attached to the uterus in a sessile manner, but frequently there is a well developed pedicle which in some cases becomes extremely attenuated. The tumor derives its blood supply through the pedicle, and it is evident that a slight degree of torsion or pressure on the pedicle may interfere seriously with the supply of nourishment. For this reason hyaline and cystic degeneration is much more frequent than in

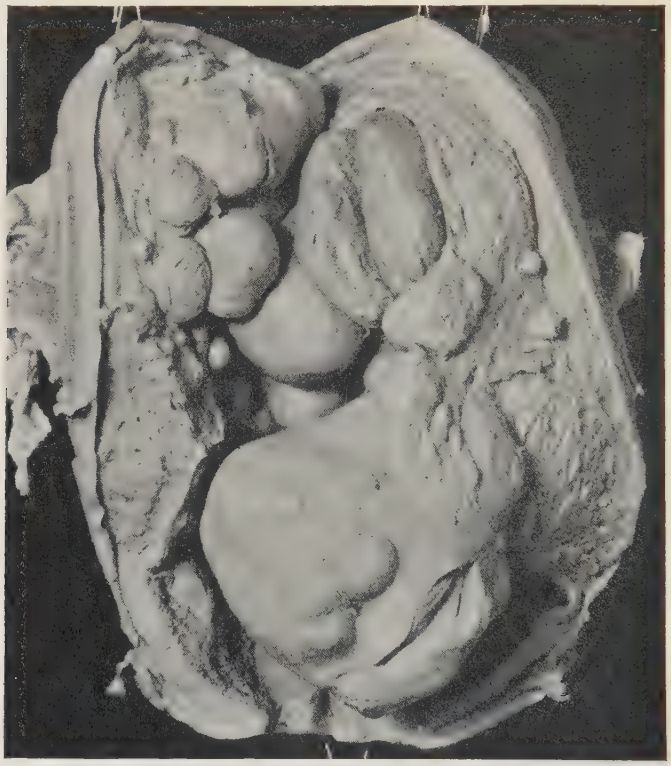

FIG. 168.—Fibroids of uterus. Multiple tumors of varying size causing great enlargement of the uterus.

the other two varieties. As a rule subperitoneal fibroids are remarkably free from adhesions, but occasionally it happens that connections are established with surrounding structures of which the most important is the omentum. In this way the tumor acquires a second source of blood supply, which, in the rare cases where the attachment to the uterus is severed becomes the only source. To such tumors the name parasitic fibroids is given. When the abdomen is opened in these cases of omental attachment the appearance may be very striking, for not only are the epiploic vessels much enlarged but the lymphatics

may be greatly distended, so that the surgeon sees the dark red color of the arteries, the deep blue of the veins, and the pale yellow of the distended lymphatics. In subperitoneal fibroids the muscle is often almost entirely replaced by fibrous tissue in which, as has already been remarked, degenerative changes are of frequent occurrence.

The *submucous fibroid* is naturally the variety most likely to produce symptoms, even when quite small in size. The tumor is usually single,

Fig. 169.—Fibroids of uterus. All three varieties are shown. The submucous fibroid protruded through this os as a large polypus.

but in some exceptional cases the cavity of the uterus may be crowded with numerous small tumors, the contiguous surfaces of which may be faceted like multiple calculi in a gall bladder. Owing to the uterine contractions the fibroid tends to become more and more polypoid, until finally it may be extruded into the vagina. Complete spontaneous separation of the pedicle is a very rare event. The submucous fibroid has escaped from its capsule and is covered only by the endometrium, from which it derives the greater part of its blood supply.

When extruded through the external os its surface is peculiarly liable to ulceration and infection, and sloughing of the entire tumor may occur. Occasionally, however, the epithelium of the investing endometrium may become thickened and squamous in character, although remaining columnar in the glands. A soft, submucous fibroid gradually enlarging and distending the uterus may closely simulate a pregnancy, and even when the abdomen is opened it may be almost impossible to differentiate the two conditions. To add to the difficulty a corpus luteum of considerable size may be present in one of the ovaries. When the cavity of the uterus is occupied by a fibroid the

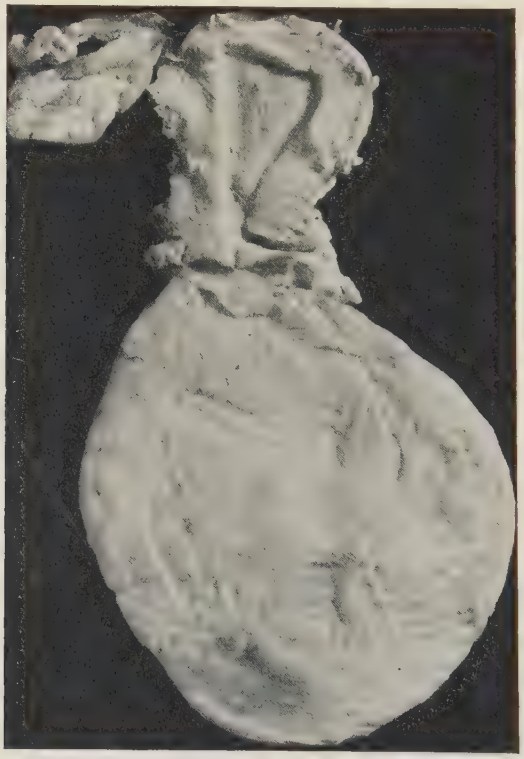

FIG. 170.—Large fibroid of cervix uteri. The uterus is perched upon the top of the tumor.

endometrium is always thickened, sometimes to a remarkable degree, and there may be extensive hemorrhage in the stroma. Similar changes, although to a lesser extent, may be present in some interstitial fibroids. They are responsible for the leucorrhea and menorrhagia characteristic of the disease.

Cervical Fibroids.—From 6 to 8 per cent of fibroid tumors occur in the cervix. The tumor is always single, although it may be associated with fibroids of the body of the uterus. It may be *interstitial*, arising

usually from the posterior wall, at first spherical but later oval, and growing upwards with the body of the uterus perched as a small mass on the summit of the tumor.

Or it may be *subperitoneal*, in which case it grows out into the broad ligament, and produces great distortion, flattening, and elongation of the uterus. The dangers of cervical fibroids, should the patient become pregnant, need no emphasis.

Degenerative Changes.—Fibroid tumors, particularly those of the subperitoneal variety, are peculiarly liable to degenerative changes.

Atrophy may occur after the menopause, due probably to the withdrawal of the ovarian stimulus. A similar result may sometimes be

FIG. 171.—Fibroid of uterus complicating pregnancy. The impossibility of delivery is very evident.

obtained by removal of the ovaries. The tumor cells lose their power of reproduction and die.

Hyaline degeneration is perhaps the most frequent change, due to insufficiency in the blood supply. It is therefore most frequent in subperitoneal tumors with narrow pedicles. The collagen fibrils become converted into a series of interlacing trabeculæ of homogeneous appearance, and staining deeply with eosin and fuchsin. The muscle fibers atrophy and may largely disappear.

Cystic degeneration is a sequel of the hyaline change. The hyaline material becomes liquified, and numerous cyst-like cavities are formed. These are not true cysts, for they possess no epithelial lining. Moreover the fluid contents, although often highly albuminous, give no

reaction for mucin, or pseudo-mucin. The fluid is usually straw-colored, but may be tinted darkly with blood. There may be numerous small cysts or one large cavity.

Fatty degeneration occasionally appears about the time of the menopause. The tumor loses its whorled appearance, and the cut surface is homogeneous and of a yellow color. The muscle fibers are replaced by rows of small fat droplets staining red with Sudan III or Scharlach R. The importance of the condition lies in the fact that it is the usual precurser of calcification.

Calcareous Degeneration.—Calcification is occasionally met with in elderly patients, and may readily be recognized by means of the

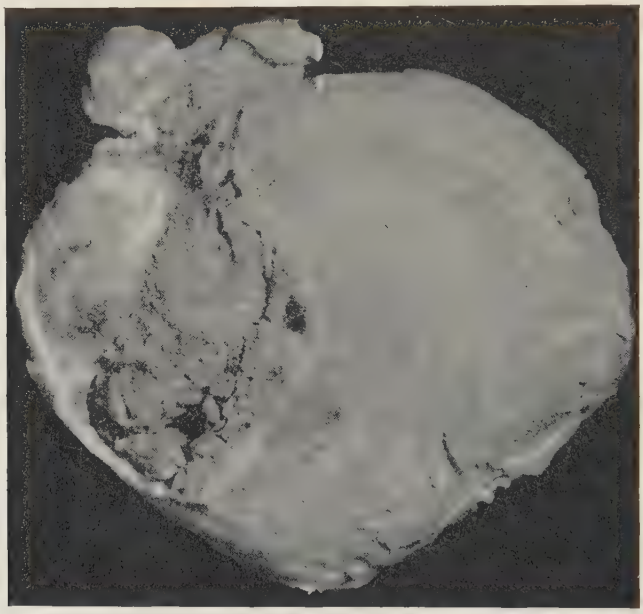

Fig. 172.—Sarcomatous degeneration of a uterine fibroid. The cut surface has completely lost its striated character and is now quite homogeneous.

X-rays. Subperitoneal fibroids are the most frequently affected. The change is preceded by fatty degeneration. The fat is broken up into glycerin and a fatty acid, and the latter unites with the calcium in the blood to form an insoluble soap, which in turn is converted into the carbonate and phosphate of calcium. Sometimes the entire tumor is calcified, sometimes only the outer shell.

Red degeneration is a peculiar change characterized by the sudden onset of pain and tenderness in the tumor. The fibroid, which is usually quite soft, varies in color from a pink to a mahogany-brown, and on section has been likened to a raw beefsteak. The condition is usually associated with pregnancy, but cases have been recorded in spinsters at the menopause. The degeneration is a rapid necrosis due

to the action of autolytic ferments converting insoluble tissue into a soluble form. A peculiar fishy smell is given off, owing to the formation of decomposition products. The red color, which is merely incidental, appears to be due to hemolysis from the lipoid substances produced. On the other hand, thrombosis of the veins is often a prominent feature, and it has been suggested that the condition may be analogous to a red infarct. This type of degeneration may occur in any variety of fibroid, but is most frequent in the interstitial form.

Sarcomatous Degeneration.—Sarcomatous metaplasia occurs in from 1 to 2 per cent of uterine fibroids.

In a well marked case the condition is readily recognized from the gross appearance, for the sarcomatous part is sharply differentiated from the surrounding fibroid. It is soft, much yellower than the white tissue of the fibroid, and the surface is homogeneous instead of whorled. Degeneration cysts may be present. The malignant change commences in the part of the fibroid furthest from the blood supply, that is the center. The earlier stages can not be recognized by the naked eye, and need the microscope for their detection.

The malignant metaplasia may affect either the fibrous tissue or the muscular tissue elements of the tumor. Thus we may speak of a fibrosarcoma and a myosarcoma, although strictly speaking the term myosarcoma is inaccurate, for a true sarcoma arises only from connective tissue. In both cases the cells and their nuclei are large, and have an appearance of active growth; mitotic figures are common. The last-named is the most important single factor in determining the presence of malignancy. It is evident that in some cases it will be extremely difficult to determine whether or not the condition should be regarded as malignant.

ADENOMYOMA

One of the most interesting tumors in the body is the adenomyoma. As the name implies it consists partly of glandular, partly of muscular and fibrous tissue. It is a fibroid containing uterine mucosa. Adenomyomata are not confined to the uterus, but also occur in the recto-vaginal septum, tubes, round ligaments, utero-ovarian ligaments, utero-sacral ligaments, sigmoid flexure, rectus abdominis muscle, umbilicus, and large quantities of normal uterine mucosa are occasionally found in the ovary. The tumor is not a common one, but is perhaps not so rare as generally supposed, for very many must be missed. Cullen, our greatest authority on the subject, described 56 cases as long ago as 1908.

Etiology.—The amount of discussion regarding the exact nature and etiology of uterine adenomyomata which has taken place since von Recklinghausen first put forward his views in 1896 is remarkable. Many theories have been propounded to explain these curious growths, but we feel that it may be said with justice that no one theory will explain every case. The one which is based on the surest foundation of observed fact is that of Cullen, who traced the origin of the mass

of new mucosa to the already existing endometrial glands. Von Recklinghausen believed that the epithelial elements of the tumor arose from portions of the Wolffian body which had become separated in early fetal life. It has also been suggested by Iwanoff that the glandular structures are formed by a downgrowth of the peritoneum which has undergone metaplasia with conversion of its flattened epithelium into columnar epithelium as the result of chronic inflammation. From whichever tissue the tumor originates, chronic

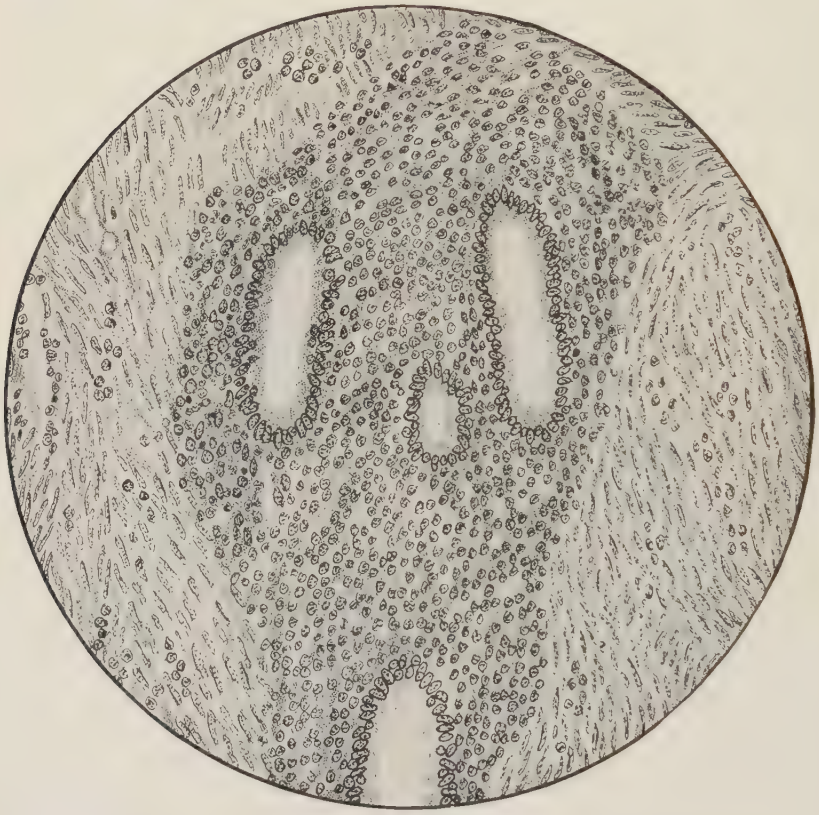

Fig. 173.—Adenomyoma of uterus. The mucosa has invaded the muscular coat to a great depth. (Graves.)

inflammation may well play an important part in determining its growth into the uterine wall.

Cullen's endometrial theory is that which is universally accepted at the present day for the great majority of cases. Not only can the continuity of epithelium between tumors and endometrium be demonstrated in serial sections, but areas of blood suggesting a menstrual function may be present, and decidual areas have been found in one case dying shortly after labor and in one case of tubal pregnancy.

Three varieties of uterine adenomyoma may be distinguished: (1) diffuse adenomyoma of the uterine body, (2) subperitoneal and intraligamentous growths, (3) submucous growths.

Diffuse Adenomyoma.—The tumor may be limited to the anterior or posterior wall or may form a mantle just outside the mucosa. Although the uterus may be enlarged to two or three times its normal size, and the affected part may be markedly thickened, the normal outline of the organ is usually retained. When the uterus is opened the diagnosis can often be made from the gross appearance. The anterior or posterior wall is diffusely thickened, with a complete absence of the sharp demarcation so characteristic of the ordinary fibroid. The thickened portion of muscle is coarsely striated, and homogeneous translucent areas resembling mucous membrane may be scattered through it. These areas often present a brownish discoloration due to the presence of extravasated menstrual blood. Small cystic spaces filled with chocolate-colored contents may be scattered throughout these mucosal areas. The line of demarcation between the tumor and the normal mucous membrane is always sharp; the tumor extends to, but never into, the endometrium.

Microscopically, the growth is made up of fibromyomatous tissue, only differing from that of an ordinary fibroid in that it is not encapsulated, together with glandular structures. The latter resemble the normal endometrium, although not so regular in appearance. "The uterine mucosa is often of normal thickness and looks perfectly normal, but as we approach the underlying diffuse myomatous tissue the mucosa is seen to penetrate it in all directions, sometimes as an individual gland, but often large areas of mucosa are seen extending into the depth. In favorable sections one can follow a prolongation of the mucosa half way through the uterus" (Cullen).

Subperitoneal and Intraligamentous Adenomyoma.—These are both peripheral growths. A tumor originating above the center of the uterus and growing outwards becomes subperitoneal, whereas one originating below the center and growing outwards will probably develop between the folds of the broad ligament and thus become intraligamentous.

These tumors are sessile, and frequently contain cysts. The cysts, which are filled with chocolate-colored fluid, may attain a great size, and as many as seven liters have been removed from one. It is possible that some of these peripheral growths are derived either from Wolffian rests or from peritoneal metaplasia.

Submucous Adenomyoma.—Little need be said about this form. It is merely a diffuse growth which has become polypoid, and presents the same structure as the diffuse variety, except that cyst formation is rarely observed.

CANCER OF THE UTERUS

The uterus is one of the organs most frequently affected by carcinoma. Cancer of the uterus and cancer of the breast are of about

equal frequency. It is commonest between the ages of 45 and 55, at a time when the uterus is undergoing involutionary changes, and is very rare before the age of 30. Although speculation with regard to the etiology of cancer is useless in the present state of our knowledge, there is one factor of extreme importance in the production of cancer of the cervix, the common form of uterine cancer. Over 96 per cent of the cases occur in women who have borne children, and it is an interesting fact that the fecundity of patients who eventually develop this form of cancer is above the average. The connecting link appears undoubtedly to be the injury to the cervix during childbirth.

Some of the anatomical and physiological distinctions between the body and the cervix of the uterus have already been pointed out, and the behavior of cancer in the two parts is so different that they deserve to be treated as separate diseases.

Cancer of the Cervix

Cancer of the cervix is much commoner than cancer of the body and much more fatal. It is almost confined to women who have borne children, and in whom there has been either laceration of the cervix, or a cervical erosion, two conditions the pathology of which is very similar. The disease commences in a very insidious fashion, and is usually well advanced before a diagnosis is made.

Gross Appearance.—As in the stomach, the lip, and other positions, cancer of the cervix may take one of three forms:

1. It may extend on the surface, forming a large, fungating, cauliflower-like mass which projects into the cavity of the vagina. This variety usually arises from the lip of the external os, and shows little tendency to invade the deeper tissues. It is therefore of limited malignancy, although alarming in appearance, but it may set up contact growths in the vaginal wall. Ulceration occurs readily, and hemorrhage especially after coitus is an early symptom.

2. It may extend deeply in the direction of the internal os, causing enlargement of the cervix as a whole, and eventually producing a deep ragged cratiform cavity, lined with crumbly sloughing débris which bleeds at a touch. This is the commonest and at the same time the most malignant form, giving rise to widespread infiltration of the surrounding tissues and early involvement of the lymphatic glands.

3. The least common form is that in which a flat indurated ulcer is produced which tends to spread superficially, and is of comparatively slow growth. It is found chiefly in elderly patients.

Microscopic Appearance.—Cancer of the cervix is usually described as a squamous-celled carcinoma, but it is by no means a typical epithelioma such as is found in the lip. There are three types of epithelium from which theoretically it may arise, (1) the squamous epithelium of the vaginal portion, (2) the thickened epithelium covering a cervical erosion, and (3) the columnar epithelium lining the cervical canal. By the time that the condition is recognized it is usually impossible to tell either from naked eye or microscopic examination what was the exact

starting point of the growth. The superficial cauliflower-like form may well arise from the epithelium of the vaginal portion, but the other two varieties arise either from the epithelium lining the canal or from the thickened layers covering an erosion.

Branching columns of cells grow down into the deeper tissues, and form large masses of squamous cells showing numerous mitotic figures, but as the growth usually originates from columnar and not from squamous epithelium there is, except in rare cases, complete absence of the cornification and cell nests characteristic of an epithelioma. The center of the cellular masses may degenerate and become liquified, with the formation of gland-like spaces, which have led to a mistaken diagnosis of adenocarcinoma. On account of ulceration,

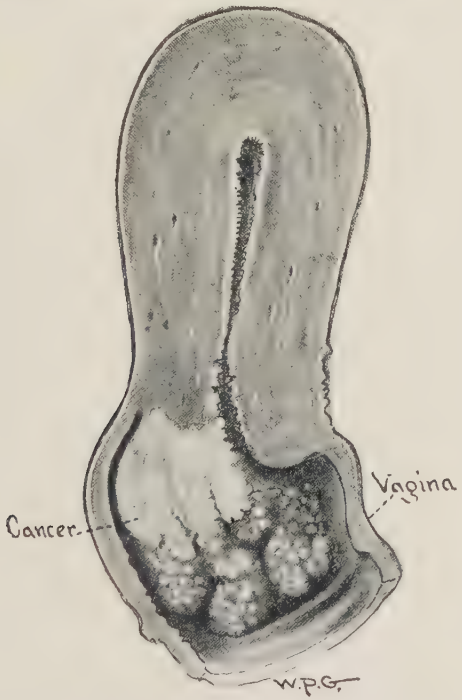

FIG. 174.—Carcinoma of the cervix. An example of the fungating but less malignant form of growth. (Graves.)

which is usually extensive, much of the microscopic picture may be obscured by an inflammatory reaction. In examining a section of the growth, therefore, care should be taken to select the growing edge of the tumor. Even without ulceration there is frequently a marked infiltration of round cells and plasma cells around the deeper parts of the growth.

In rare cases an *adeno-carcinoma* is formed instead of a squamous-celled carcinoma. The growth probably arises from the epithelium

of the cervical glands, and the microscopic picture is quite typical. The tumor does not display the invasive tendency of the squamous-celled form, so that the results of operative interference are much more favorable.

Spread.—The malignancy of cancer of the cervix is due to its invasive character. The local condition may be readily removed, but only too often the surrounding tissues have already become infected.

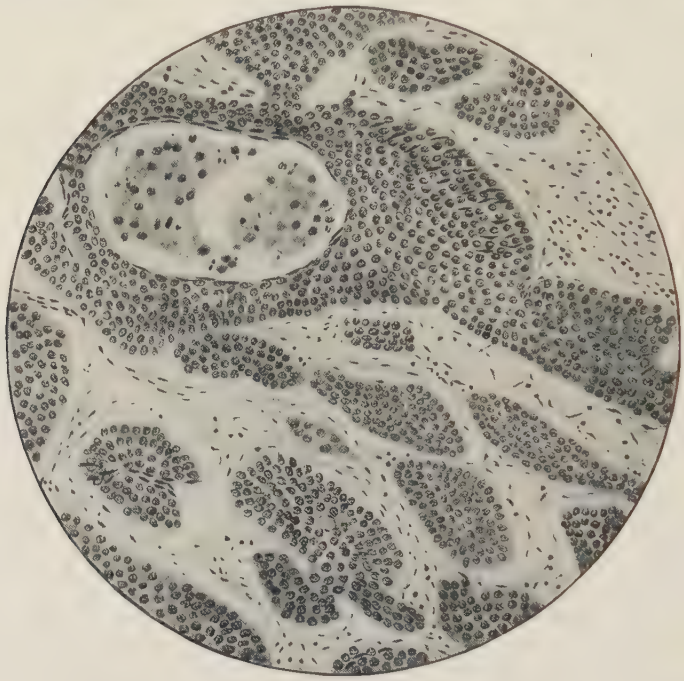

Fig. 175.—Carcinoma of cervix uteri. The gland-like space is due to degeneration. The absence of mitotic figures is a quite unusual feature.

The spread may be (1) by lymphatic spaces, (2) by lymphatic vessels, or (3) by the blood stream.

Permeation of the lymphatic spaces in the connective tissue, with which the cervix is so richly supplied, is the chief method of spread. Columns of cells creep along these spaces and soon reach the cellular tissue of the parametrium. From there the spread continues forwards to the bladder, backwards through the utero-sacral ligaments to the rectum, and downwards into the vagina. Upward spread into the cavity of the uterus is remarkably rare, the line of the internal os appearing to act as a barrier to the growth.

Spread by the lymphatic vessels with involvement of the lymphatic glands is somewhat capricious. An early case may show extensive glandular involvement, but on the other hand an advanced and inoperable case may show little or none. As with other ulcerating tumors the glandular enlargement may be inflammatory and not malignant.

The usual order of involvement is the glands at the base of the broad ligament, the iliac group, the hypogastric group, and the sacral group. The nearest glands may be passed by, however, and secondary growths set up in a more distant group.

Spread by the blood stream is a very late complication, and only occurs in the most advanced cases.

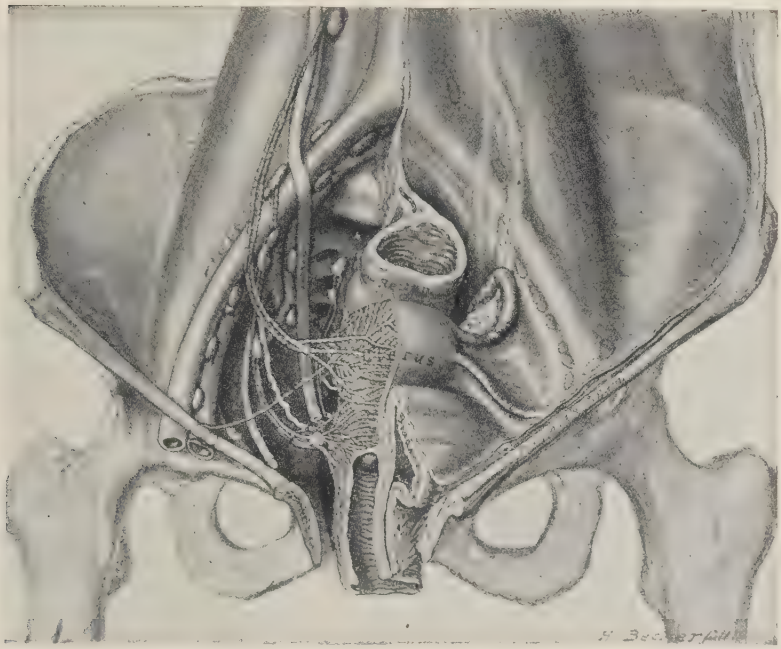

FIG. 176.—Schematic representation of the cervical and fundal lymph-channels, with the location of the various lymph-glands which may be involved in cancer. (Kelly and Noble.)

CANCER OF THE BODY

Cancer of the body forms less than 10 per cent of all cases of cancer of the uterus. It occurs later in life than cancer of the cervix, and on that account is usually diagnosed at an earlier date, for as the characteristic hemorrhage occurs after the menopause it is more likely to arouse the alarm of the patient. In sharp distinction to cancer of the cervix it is even more frequent in nulliparous women than in those who have borne children. An association of cancer of the body with fibroids is by no means uncommon, whereas it is distinctly rare in cancer of the cervix.

Gross Appearance.—The tumor arises from the endometrium, usually in the region of the fundus, and the direction of the growth is at first superficial rather than deep, so that a large cauliflower-like mass comes to occupy the cavity of the uterus. This may be attached to the uterine wall by a more or less narrow base, and in

some cases it may become definitely pedunculated, but it is much more usual for it to extend over the endometrium, so that numerous soft sessile masses project from the wall into the cavity. Although spread into the cervical canal might be expected it is of very rare occurrence, and the disease is confined strictly to the body of the uterus. With the progress of the disease the muscular wall becomes infiltrated, but involvement of the parametrium is never early as in cancer of the cervix. The body of the uterus is enlarged, but only to a moderate extent. Ulceration is not common, so that the general symptoms of an infected neoplasm, so characteristic of the later stages of cervical cancer, are rarely seen in this condition.

Fig. 177.—Carcinoma of the body of the uterus. A large area is covered by the growth, but there is no visible invasion of the muscle.

Microscopic Appearance.—Cancer of the body is an *adenocarcinoma,* arising from the columnar epithelium covering the surface or lining the glands of the endometrium. The appearance may vary somewhat. Usually the growth is made up of numerous branching tubular glands separated by a scanty stroma. The lining cells are tall and columnar, and when several layers in depth and irregular in arrangement the malignant character of the condition is quite evident. When a portion of the muscle is present in a scraping the new-formed glands can be seen invading the wall deeply, and the diagnosis is beyond doubt. In some cases, however, the tubules are well formed

and lined by but a single layer of columnar cells. If the muscle wall is not present in the scraping the diagnosis may be a matter of considerable difficulty. In such a case particular attention must be paid to the nuclei of the lining cells. In a normal gland these are all situated at the same level, and are of regular shape and staining properties; the cells are limited by a basement membrane. In carcinoma the nuclei are arranged at different levels, vary in size, some stain dark and others light, and mitotic figures may be seen; there may be no basement membrane.

Sometimes the appearance is that of a *carcinoma simplex* rather than of an adenocarcinoma, owing to the gland spaces becoming packed

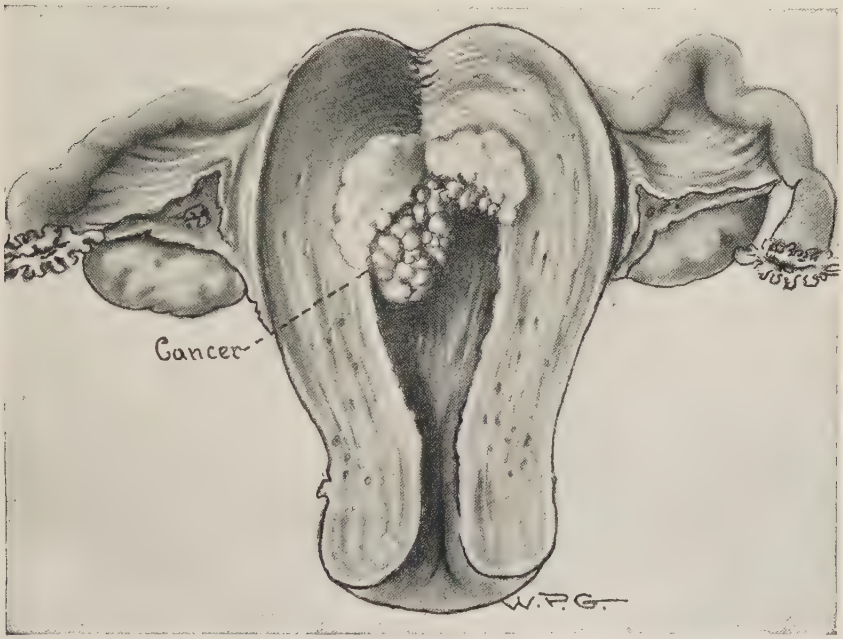

Fig. 178.—Adenocarcinoma of the body of the uterus. The disease is beginning in the upper part of the canal and is extending both inward into the muscular wall and outward toward the canal. In this case the growth has a papillary appearance. (Graves.)

with proliferating cells. This variety must always be regarded as more malignant than that of the more simple tubular form.

Very rarely a *squamous-celled carcinoma* may be found, arising, it is supposed, from a patch of leukoplakia, the result of a chronic endometritis.

Spread.—Cancer of the body has not the same powers of infiltration as cancer of the cervix. It is more amenable, therefore, to operative treatment. But although growth is at first centripetal rather than centrifugal, invasion of the muscular wall steadily goes on until, at a somewhat late date, the parametrium is reached. In some cases the growth may pass out along the Fallopian tube and infect the ovary.

The lymphatic glands at the side of the vertebral column may be involved late in the disease, and blood spread with metastases in the internal organs is also a terminal manifestation.

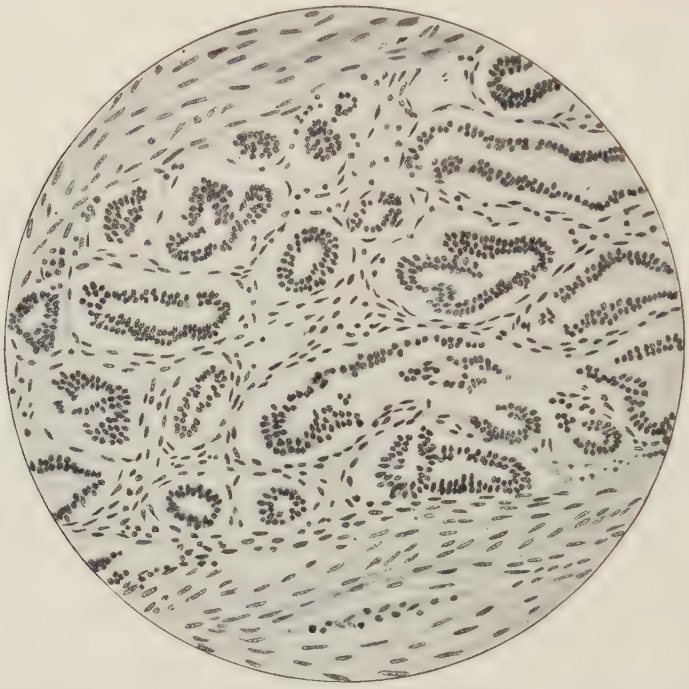

FIG. 179.—Adenocarcinoma of the body of the uterus. The newly formed and irregular glands are invading the muscularis.

SARCOMA OF THE UTERUS

Sarcoma of the uterus may occur as a malignant degeneration of a preexisting fibroid; this is much the most common form, and has already been described on page 491. Or it may occur *de novo* as a distinct rarity. It is the latter form which is discussed here. In contradistinction to carcinoma of the uterus, the condition is much more common in the body than in the cervix.

The tumor may arise: (1) in the uterine wall, (2) in the endometrium.

Sarcoma of the uterine wall may be diffuse or circumscribed. The diffuse form, so rare that it need not be considered here, produces a soft uniform enlargement like that of the pregnant uterus.

The circumscribed sarcoma commences in the uterine wall, but often becomes submucous and pedunculated. These uterine polypi may be removed a number of times before their true nature is recognized, and are apt to be regarded as recurring fibroids. The gross appearance is similar to that of a sarcoma arising in a fibroid, and is

such as at once to arouse suspicion. It is soft, even brain-like, homogeneous, yellowish-pink in color, and frequently shows hemorrhages and cyst formation. It will be noted how much the tumor differs from the ordinary fibroid. Microscopically the tumor is made up of round cells or spindle cells.

Sarcoma of the endometrium differs in no important particular from sarcoma of the uterine wall. It may be diffuse or circumscribed, and the appearances are those already described. The line of division between the thickened mucosa and the muscular wall is curiously well maintained.

A very remarkable and interesting form of sarcoma of the endometrium is the *grape-like sarcoma of the cervix*. This tumor is peculiar in that it may occur at any age, even in infancy. It springs from the cervical canal or the vaginal portion of the cervix, and projects into the vagina as a group of polypoid masses, often likened to a bunch of grapes. The cyst-like appearance of the masses is due to edema of the sarcoma. The cells are round or spindle shaped, but striated muscle fibers have been described, and by some the condition is regarded as a rhabdomyoma.

Fig. 180. Grape-like sarcoma of cervix. This specimen was removed from a child one year of age.

The spread of sarcoma of the uterus is both local and general. The disease tends to spread throughout the uterus and to invade the parametrium, although the latter tendency is not so marked as in carcinoma of the cervix. In the later stages there is blood spread with involvement of the lungs, liver, and other distant organs.

CHORIONEPITHELIOMA

One of the most remarkable tumors in the body is the chorionepithelioma, which usually commences in the uterus, although cases have been described occurring in the Fallopian tube, the ovary, and even in teratomatous tumors of the testicle. The tumor is unique in that it is derived not from the tissues of the patient but from those of another individual, for it arises from the cells covering the chorionic villi.

The condition comes on after pregnancy or even more frequently after an abortion. In about one third of the cases the preceding pregnancy terminated in the formation of a hydatidiform mole. It is difficult to say exactly how great is the danger of a hydatid mole being followed by chorionepithelioma, but it has been estimated that in about

15 per cent of cases this malignant change may occur. Both chorionepithelioma and hydatidiform mole are frequently associated with a remarkably large, sometimes bilateral, corpus luteum, an organ the function of which appears to be to stimulate the activity of the syncytial covering of the chorionic villi, and thus ensure the firm fixation of the embryo to the uterine wall.

The onset of the growth may be soon after the termination of pregnancy, so soon indeed, as to suggest that the symptoms may be due to retained products of conception. At other times, however, many months or it may be years may elapse between the appearance of the tumor and the date of the last pregnancy.

Gross Appearance.—The tumor usually commences at the fundus of the uterus at the placental site. When an early case is examined it is found that the first appearance of the growth is not in the endometrium but in the muscular wall itself. Extension takes place into the cavity of the uterus and to a lesser extent into the muscular wall, so that a soft, hemorrhagic, maroon-colored mass is formed which causes moderate enlargement of the uterus. There is a curious tendency to the formation of implantation growths, sometimes on the lower part of the uterine wall, sometimes even on the wall of the vagina. In course of time the tumor may appear on the peritoneal surface of the uterus.

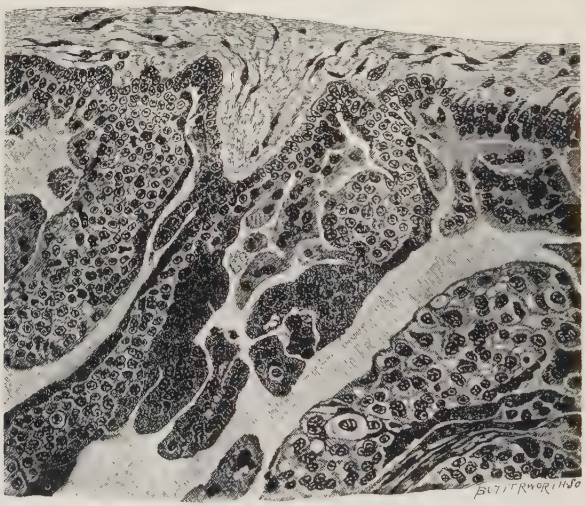

Fig. 181.—Chorionepithelioma. Most of the cells are the clear Langhans' cells. In addition, there are a few dark syncytial masses. (Keen after J. H. Teacher.)

Microscopic Appearance.—In order to understand the microscopic appearance brief reference may be made to the structure of a normal chorionic villus. The villus is covered by the trophoblast, of fetal origin, consisting of two types of epithelial cell, an inner layer of small cubical clear cells with large pale nuclei, the Langhans' cells, and an

outer layer of dark undifferentiated protoplasmic masses with dark nuclei, the syncytial layer. Both of these layers are invasive in function, and therefore readily penetrate the walls of blood vessels.

The chorionepithelioma consists of irregular masses of Langhans' cells closely packed together, with here and there the darked multinucleated syncytial elements. There are no regular stroma nor blood vessels, the tumor cells deriving their nourishment from the blood with which they are so abundantly bathed.

The recent work of Ewing, Geist, and others has shown that chorionepithelioma does not represent a uniform clinical and pathological picture. Some cases run a benign course, others an intensely malignant one. Two main varieties may be distinguished, between which, however, there are many intermediate grades which add greatly to the complexity of the subject and to the difficulties of diagnosis. The first is the typical chorionepithelioma of Marchand which may be called a choriocarcinoma; the second is the atypical chorionepithelioma of Marchand, which may be called a syncytioma.

The characters of the *choriocarcinoma* are those which have just been described. It is a true malignant tumor, with markedly invasive properties, and a great tendency to set up metastases. Both syncytial and Langhans' cells are always present. Even in this variety abdominal hysterectomy offers fair chances of success.

The *syncytioma* is also a true tumor, but with markedly regressive tendencies, and it does not set up secondary growths, although it may produce abundant hemorrhage from local invasion. It consists of groups and islands of syncytial cells, often giant cell in type, but the bulk of the mass is made up of blood clot and necrotic tissue. No Langhans' cells are present. Its regressive character is evidenced by the spontaneous disappearance of the tumor which sometimes occurs. Even in the more malignant varieties of chorionepithelioma, however, this particular regressive tendency may manifest itself, for not only the primary growth but even the metastases may disappear in the same mysterious manner, a remarkable process which may actually be watched in the case of metastatic nodules on the vaginal wall.

If a definite diagnosis of syncytioma can be made from the uterine scrapings a conservative line of treatment may be adopted. Often, however, intermediate varieties take the place of the two main clear cut forms, and in such cases thorough removal by hysterectomy is the only safe course.

The Fallopian Tubes

It would almost appear as if nature had designed the Fallopian tubes to become the seat of an infective process, and were this the case the attempt has certainly been a successful one, for few organs are more frequently affected by inflammation, both acute and chronic. The tube is open at both ends, so that infection may enter from either end, as well as through the blood stream. The uterine outlet is extremely narrow and may readily become blocked by swelling of the

mucosa, so that efficient drainage is impossible. Finally the innumerable folds of the mucosa are admirably adapted to harbor microorganisms for long periods of time.

The most important pathological condition affecting the tubes is inflammation. Tumors are rare and of minor importance.

Salpingitis or inflammation of the tubes may be due to pyogenic bacteria or to the tubercle bacillus. These two varieties differ in several important particulars and will, therefore, be considered separately. By far the most frequent pyogenic cause of salpingitis is the gonococcus, which is responsible for about 75 per cent of all cases. In puerperal sepsis the streptococcus may readily infect the tube.

Some conclusions from a recent paper by Curtis on the bacteriology of the Fallopian tubes are of interest. He found that in a series of 300 cases of salpingitis 70 per cent were certainly and 10 per cent were probably due to infection with the gonococcus, 15 per cent to other pyogenic organisms, notably various types of streptococci, and 5 per cent to the tubercle bacillus. B. coli was frequently found in tuboovarian abscesses of large size, but as a primary cause of salpingitis neither the colon bacillus nor the staphylococcus were of importance. Gonococci were never obtained in culture more than two weeks after the subsidence of the fever. The Fallopian tube, therefore, does not appear to be a focus for chronic gonorrheal infection, and persistently active gonorrhea of the tubes is due either to recurrence of infection from without or to repeated invasion of bacteria from the chronically infected lower genital tract. On the other hand streptococci of various types were isolated many months or even years after the introduction of infection.

GONORRHEAL SALPINGITIS

The gonococcus may reach the tube soon after the initial infection, or a long interval may elapse. The latter cases are probably due to a latent infection in the cervix awakening to fresh activity. The infection, which is practically always bilateral, may be mild, giving rise to a catarrhal salpingitis, or virulent, in which case a purulent salpingitis results. In the catarrhal form there is little structural alteration in the tube, apart from swelling of the mucosa, but with repeated attacks the ends of the tube may become closed and a hydrosalpinx is formed.

Hydrosalpinx.—The ostium of the tube may become closed in two ways; (1) Owing to the chronic inflammation the fimbriæ no longer project freely from the margin of the opening but become drawn into the mouth of the tube, adhere together, and effectively close the opening. (2) The inflamed fimbriæ may become adherent to the ovary or other neighboring structures, and again the mouth of the tube becomes sealed. The extremely narrow uterine end, which is less than 1 mm. in diameter, is readily closed by the inflammatory swelling, and the tube is effectively sealed. The serous secretion of the lining cells gradually distends the tube, and a hydro-

salpinx is formed. The distension is always more marked at the distal end, and as the peritoneal covering is not so elastic as the rest of the wall, the distended tube becomes curved into a characteristic retort-like form. The walls are thin and may be translucent, for the

FIG. 182.—Hydrosalpinx. The ostium of the tube is so completely closed that no trace of it can be detected.

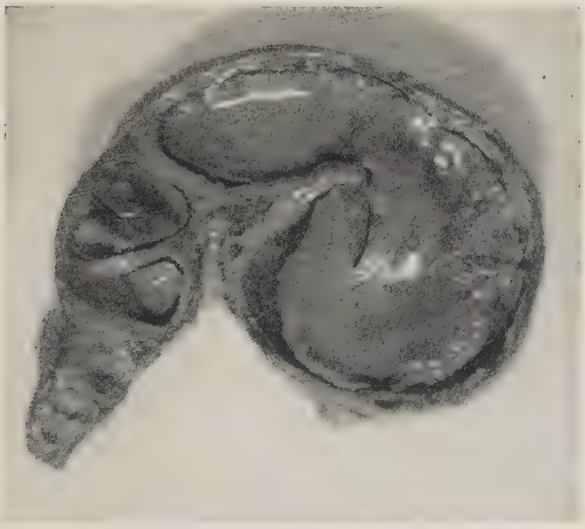

FIG. 183.—Pyosalpinx showing the characteristic retort shape.

muscular coat has not been affected and thickened by the inflammatory process. The mucous membrane becomes extremely atrophied. The contents are clear, watery, and albuminous.

Pyosalpinx.—If the infection is a more virulent one a suppurative process is set up. The entire wall, both mucosa and muscularis, is invaded with inflammatory cells, at first polymorphonuclears, but later lymphocytes and plasma cells. The latter are particularly characteristic of chronic salpingitis. The tube is filled with pus. If the ends do not become sealed off the result is a *pus-tube*, with thickened walls and purulent contents. If, on the other hand, the ends are closed a *pus-sac* or pyosalpinx is formed, the walls of which consist of thickened connective tissue with but little muscle, whilst peritoneal adhesions are almost invariable. The pus obtained at operation is usually sterile, for the infecting bacteria have long since died out, but in more recent cases the gonococcus may be recovered. Secondary infection with Bacillus coli is not infrequent, in which case the pus will have the characteristic coli smell.

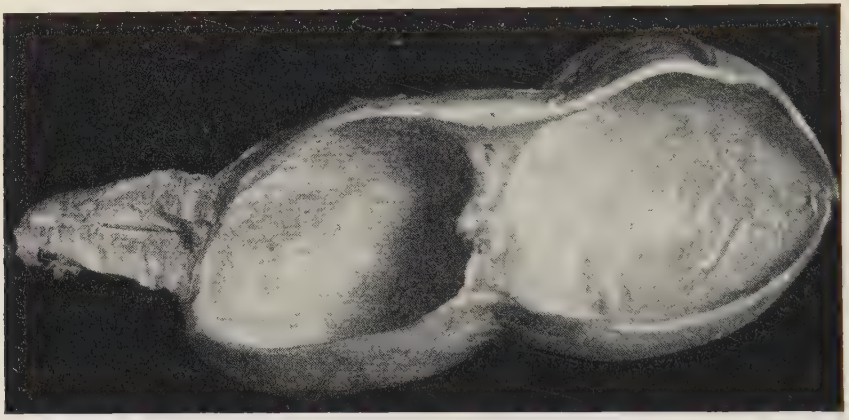

Fig. 184.—Pyosalpinx with occlusion of proximal end of the tube. Although the tube was a bag of pus the patient had no symptoms and the condition was only discovered accidentally.

Tubo-ovarian Abscess.—That the fimbriæ when inflamed may become adherent to the surface of the ovary has already been pointed out. In such an event it is obvious that any infective material in the tube will have ready access to the ovary. Under ordinary conditions the thick tunica albuginea forms an efficient protection to the ovary, but at the time of the rupture of a ripe Graafian follicle the path is open for any organisms to invade the ovary, and the soft hemorrhagic tissue of the corpus luteum forms an excellent culture medium. In this manner an abscess in the ovary is formed, which may gradually extend until it involves practically the entire organ, whilst it communicates with the pus-sac by an opening which is usually quite narrow. Such a condition is called a tubo-ovarian abscess.

Nodular Salpingitis.—Occasionally in gonorrhoreal salpingitis but more frequently and to a greater degree in the tuberculous form, the isthmus of the tube may be remarkably thickened and present a

curiously nodular appearance, so that the condition has been named *salpingitis isthmica nodosa*. The changes in the wall of the tube are somewhat peculiar. In addition to the usual inflammatory infiltration and edema of the muscularis the epithelial elements become pressed between the muscular fibers, where they proliferate and form new glandular spaces. These may at first communicate with the lumen of the tube, but eventually they become completely shut off, so that adenomatous-like masses are seen deep down in the muscularis. It will be readily understood that should an ovum wandering down the tube become entrapped in one of these diverticula and then impreg-

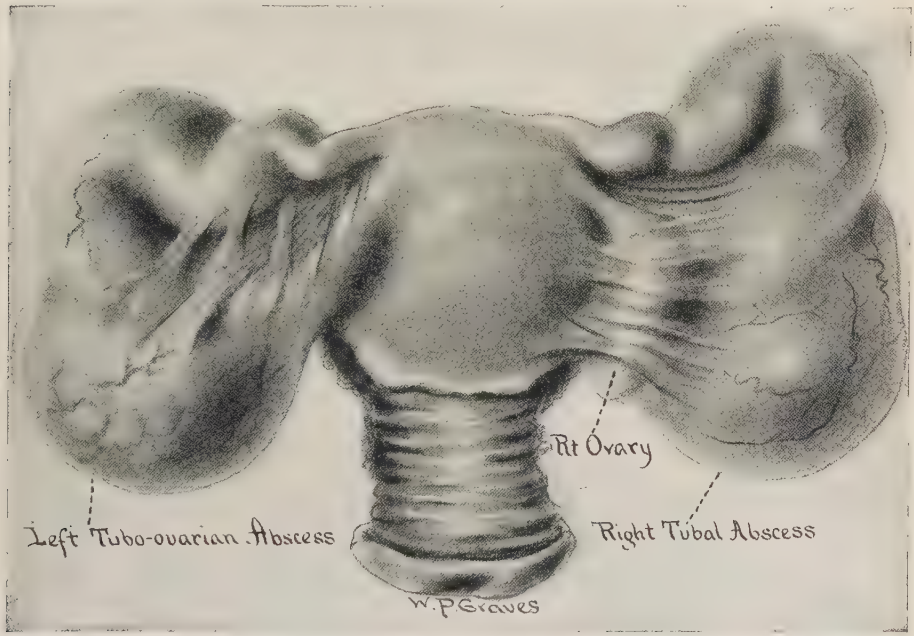

FIG. 185.—Right tubal abscess, left tubo-ovarian abscess. On the right is a tubal abscess distinct from the ovary which is seen buried in adhesions. On the left the tube and ovary are involved in a common abscess, the ovarian portion of the sac being represented with a slightly scarred surface. (Graves.)

nated, a tubal pregnancy will almost certainly result. Although this condition is not uncommon in gonorrheal salpingitis it is more characteristic of the tuberculous form.

TUBERCULOUS SALPINGITIS

Tuberculosis of the Fallopian tube is always secondary to some tuberculous focus elsewhere in the body, frequently in the lung or the bronchial glands. When once infected the tube may act as an important source of infection for the peritoneum, so that a tuber-

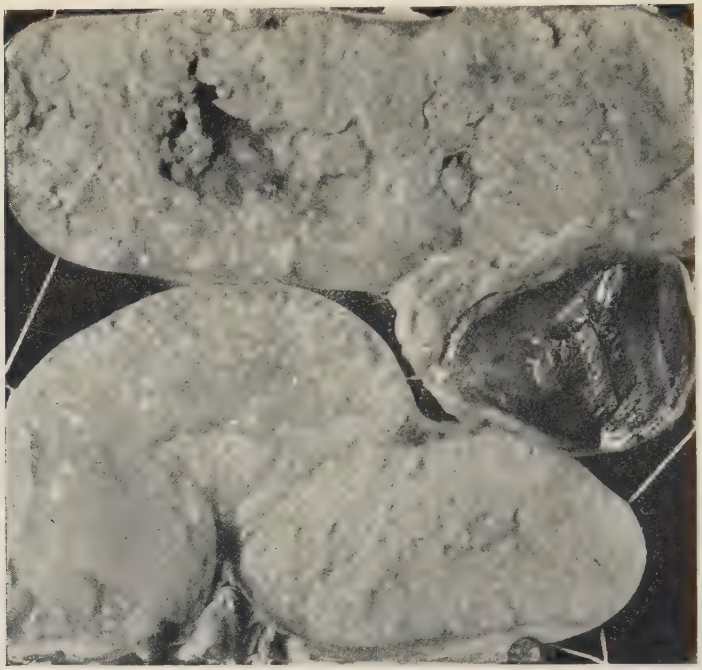

FIG. 186.—Double tuberculous pyosalpinx. The tubes are distended with pus almost gelatinous in consistence.

FIG. 187.—Tuberculous salpingitis. Tubercles of various size cover both the tube and the broad ligament. The tube is much thickened.

culous peritonitis frequently proves intractable until the tuberculous tubes have been removed.

The infection usually reaches the tubes by the blood stream, occasionally through the ostium from a tuberculous peritoneum, and almost never from the uterus. The condition is practically always bilateral.

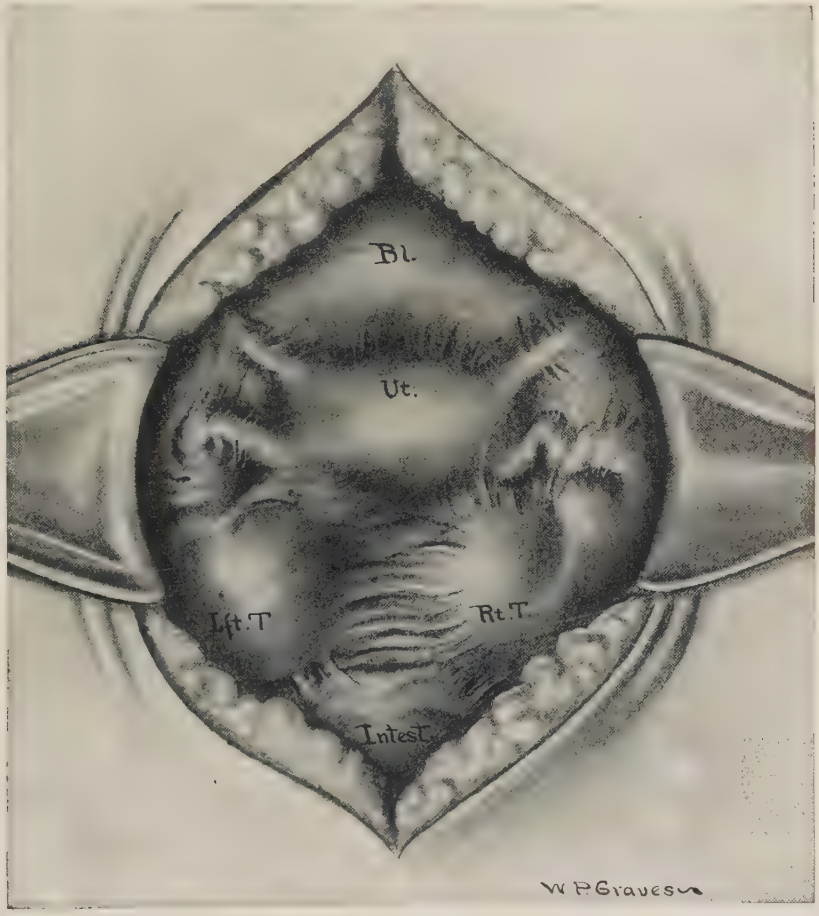

FIG. 188.—Pelvic adhesions from salpingitis. Seen through an incision with the patient in the Trendelenburg position. Bladder, uterus, tubes, and intestines are all involved and matted together in a mass of adhesions. (Graves.)

The course of the disease is very similar to that of the gonorrheal form. The ostium is closed quite early, so that a tuberculous pyosalpinx results. Only rarely does a hydrosalpinx form. The pus-sac contains material which is more inspissated and mushy than in the gonorrheal variety, and in old cases it may become quite putty-like. In the event of a mixed infection occurring the contents will

be fluid and in no way characteristic. Fibrosis of the wall is a marked feature, so that in places the lumen of the tube may be obliterated. Nodular salpingitis of the isthmus is often quite pronounced. The adhesions which are so frequent an accompaniment of tubal inflammation are often extraordinarily dense in the tuberculous variety, so much so indeed as to make removal in some cases impossible.

The *diagnosis* of tuberculous salpingitis when the abdomen has been opened may be easy or very difficult. When the serous coat is studded with miliary tubercles the diagnosis is self-evident. The small white subserous cysts which are frequently seen on the surface of the tube must not be mistaken for tubercles. These are probably due to downgrowths of the serous coat, the result of a mild form of inflammation. In other cases no tubercles can be seen, and the final diagnosis may have to depend on microscopic examination of the tube wall.

TUBAL CYSTS

Small *subserous cysts* are of common occurrence. They are no larger than a pin's head, white and glistening. They are probably formed from the peritoneum as the result of a mild form of inflammation.

Cysts of the hydatids of Morgagni are also by no means uncommon.

Fig. 189.—Tubal pregnancy. The embryo is seen lying in the dilated and thickened tube.

They are small cysts about the size of a pea, filled with clear serous fluid, and attached by a long slender stalk to one of the fimbriæ of the tube.

TUBAL PREGNANCY

Many factors may lead to the arrest of the impregnated ovum in the Fallopian tube, but by far the most important of these is a preexisting chronic salpingitis, a condition in which the folds of mucous membrane become thickened and matted together, deep glandular pockets are formed, the helpful cilia are lost, and everything conduces to entrap the ovum on its downward journey. The etiological importance of chronic salpingitis is illustrated by the fact that

the condition is rarely seen in nulliparæ, and that a long interval of sterility often supervenes between it and the last pregnancy.

The ovum may develop in any part of the tube, but the ampullary site is the commonest. When the ovum develops in the outer part of the tube the ostium usually becomes closed by the end of the second month, when in the inner part of the tube it remains open.

Decidual formation never occurs to any marked degree in the tube, and as the decidua forms one of the strongest barriers to the invasive

FIG. 190.—Tubal pregnancy showing chorionic villi at the placental site in the wall of the tube.

action of the trophoblast covering the chorionic villi, the latter is allowed free play, and burrows deeply into the tube wall. A well marked decidual reaction, on the other hand, occurs in the uterus, and in some cases this decidua is expelled as a triangular cast. The swelling of the endometrium causes the uterus to enlarge to the size of a two months' pregnancy. Uterine scrapings will show decidual cells but no chorionic villi, a finding highly characteristic of tubal pregnancy.

There are two chief modes in which a tubal pregnancy may terminate, (1) by tubal abortion, and (2) by tubal rupture. In extremely rare cases the pregnancy may go on to full term within the lumen of the tube.

Tubal abortion is much the commoner method of termination. Owing to the erosive action of the trophoblast the maternal vessels rupture into the gestation sac, converting it into a tubal mole, and the tube itself is distended with blood, a condition of hematosalpinx. Although hematosalpinx is said in some cases to be due to inflammation of a non-gravid tube, for practical purposes it may be regarded as an indication of tubal pregnancy. The mole consists of a firm mass of blood clot in which chorionic villi may be demonstrated as well as

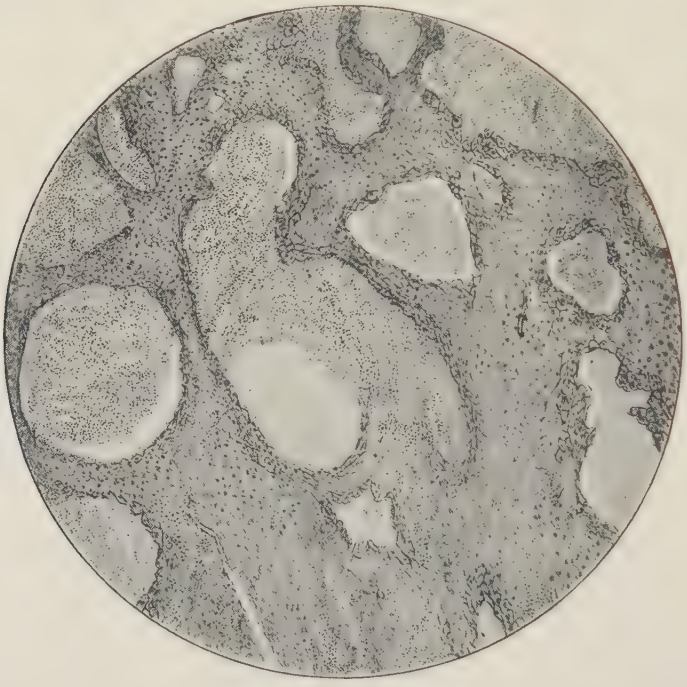

Fig. 191.—Uterine scraping from a case of tubal pregnancy, showing decidual cells and large blood spaces, but no chorionic villi. (These are formed in the tube.)

in the tube wall, but it is useless to look for fetal parts. Blood escapes through the ostium and forms a hematocele in the pouch of Douglas which can be palpated on vaginal examination. The mole itself is expelled by the muscular contractions of the tube wall before the ostium has closed at the end of the second month. In the rare cases of pregnancy in the interstitial part of the tube the mole may be expelled into the uterine cavity. Synchronously with the tubal abortion there is a discharge of blood from the uterus. This is not derived from the tube, but from the thickened and congested endometrium. At the same time shreds of decidua may be passed.

Tubal rupture occurs in about one fourth of the cases, usually about the end of the second month, and is due to the chorionic trophoblast destroying the wall of the tube and perforating the serous

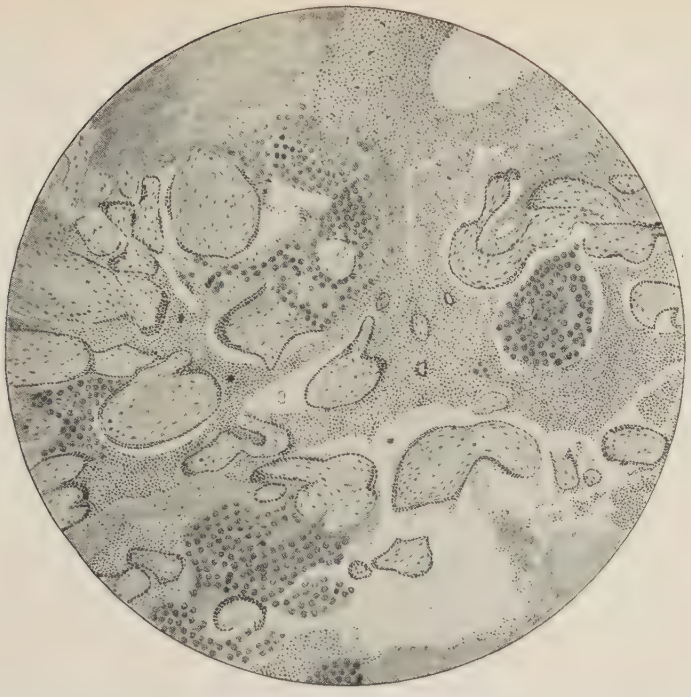

FIG. 192.—Uterine scrapings from a case of ordinary pregnancy, showing chorionic villi as well as decidual cells. For comparison with Fig. 191.

FIG. 193.—Tubal pregnancy. Hematosalpinx. (Graves.)

coat. The sudden rush of blood may constitute one variety of abdominal catastrophe, and the patient dies with symptoms of internal hemorrhage.

In rare cases the fetus may be so slowly extruded through the ostium or a rent in the tubal wall that death does not ensue, connections are formed with the surrouding viscera, and a secondary abdominal pregnancy results which may go on to full term. The fetus then dies, and becomes shrivelled up and converted into a mummified mass, in which lime salts are deposited, a condition of *lithopedion*. In a recent case in the Winnipeg General Hospital the heart sounds of a seven months fetus could be distinctly heard, but at operation the fetus was found to lie entirely between the layers of the broad ligament.

RARE CONDITIONS

Tumors.—There is no common variety of tumor affecting the tube. The most frequent is *primary carcinoma*, which takes the form of an adenocarcinoma. A curious feature is that in 35 per cent of the cases recorded it has been bilateral. The tube is distended by a soft yellowish mass. Primary chorionepithelioma has occasionally been described. Other forms of tumor are too rare to be considered here.

Syphilis is very rarely seen. It occurs in the form of gummata

The Ovary

Anatomy.—Before passing to a discussion of the pathological conditions affecting the ovary, one or two anatomical points may be briefly considered.

The stroma of the ovary is of a peculiar character. It contains no fibers, except just under the germinal epithelium or along the line of the blood vessels, and is made up of elongated and rounded cells. These cells are of two distinct types, (1) the interstitial cell allied to and arising from the germinal epithelium, (2) the connective tissue cell derived from the connective tissue of the Wolffian body and allied to the fibrous tissue group. The former possesses much of the potentiality of the oogenic tissue, the latter is but a supporting structure. All epithelial structures within the ovary, including tumors and cysts, are derived from a common source, the germinal epithelium.

The Graafian follicles, some 30,000 in number, are all present at birth, and none are formed at a later date. Of these only about 500 become converted into corpora lutea, so that 29,500 never reach full development. These follicles gradually undergo a process of degeneration or atresia, in which the membrana granulosa disappears, and from the theca interna is formed a yellow lining of cells identical with those of a true corpus luteum except that they are smaller in size. These cells are called theca-lutein cells. Such an atresic follicle is much more liable to pathological changes than the corpus luteum itself.

The common affections of the ovary are inflammation, cysts, and tumors.

INFLAMMATION

Infection may reach the ovary from the Fallopian tube or through the blood stream. The former is naturally the route of election in gonorrhea and puerperal sepsis, and is much the commoner of the two. The latter method is occasionally seen in infectious fevers, such as typhoid, mumps, etc.

Ovarian Abscess.—After the dehiscence of a Graafian follicle the ovary lies open to infection from the tube, especially as in inflammatory conditions of the tube the fimbriæ may be fused to the ovary and thus establish a direct connection between the two organs. The common cause is gonorrhea, but puerperal sepsis may also give rise to this complication. The formation of pus causes gradual enlargement of the ovary, but it is remarkable how few symptoms may develop even when the ovary is little more than a bag of pus. At first the wall of the abscess is formed by the wavy outline of the yellow lutein tissue, but in course of time this becomes invaded by nodular granulations, and the lining membrane is then of a granular faintly yellow appearance, not unlike frog's spawn. The common fusion of the tube to the ovary in inflammation renders communication between an ovarian abscess and a pus sac very easy, with the production of a tubo-ovarian abscess, a condition which has already been described.

Acute Oöphoritis.—Acute inflammation of the ovary is commonly seen as a part of puerperal sepsis, either from puerperal peritonitis or by infection through the blood stream. In rare cases it may complicate one of the acute infective fevers. Both ovaries are usually involved, and are enlarged, soft, very congested, and may contain numerous small abscesses scattered throughout the stroma, the follicles being distended with pus.

Chronic Oöphoritis.—Fibrotic changes in the ovary are of very common occurrence, but it is often impossible to say what has been the primary etiological factor. Such fibrosis, however, may usually be traced to a previous infection, either gonorrheal or puerperal. In children the appendix may act as a source of infection.

The ovaries are enlarged, although as the result of repeated attacks of salpingo-oöphoritis they may become smaller than normal. The surface is very uneven and may be deeply scarred. The greater part of the organ is made up of dense fibrous tissue with very thick-walled arteries, and here and there the fibrous remains of corpora lutea. So-called sclero-cystic disease of the ovary, the small cystic ovary, is a very common result of chronic inflammation. Both on the surface and on section numerous small cysts can be seen, with, it may be, a comparatively small amount of intervening stroma. This condition is considered in the succeeding paragraphs.

CYSTS OF THE OVARY

No organ in the body is so frequently the site of cyst formation as the ovary. These cysts vary greatly in nature. Some appear to be

the result of inflammation, retention, or degeneration, whilst others are true tumors or cyst-adenomata. The latter will be considered in connection with ovarian tumors.

Follicular Cysts.—By far the commonest variety of cyst is the follicular cyst, retention cyst, distension cyst, or hydrops follicularis. This is the cyst found in the condition already referred to as sclerocystic disease of the ovary or the small cystic ovary. The cysts are atresic follicles which have failed to rupture owing to the general fibrosis of the chronically inflamed ovary and especially to the thickening of the tunica albuginea. The relation between the cysts and chronic inflammation is, however, by no means proved. Cyst formation takes place before the follicle has begun to ripen; if the process of maturation has already commenced the result will be a lutein cyst (see below).

Fig. 194.—Lutein cysts of the ovary, with thick wavy lining of yellow lutein tissue.

It is difficult to state just at what stage the normal follicle graduates into a follicular cyst. We may say, however, that if it exceeds 1.5 cm. in diameter it should be regarded as exceeding the physiological limits. As a rule the cysts do not attain to any great size, being seldom more than 3 cm. in diameter. They may be single or multiple, and occasionally the ovary may be converted into a tumor riddled with small cysts separated by thin septa.

The cyst wall is composed of fibrous tissue lined by a single layer of epithelium. In the small cysts this may be cylindrical or cubical, but in the larger cysts it becomes flattened. The fluid is clear and of a pale yellow color. Hemorrhage is rarely observed. The ovum can not be found.

Follicular cysts may occur at any period of life up to the climacteric. They have even been described in the fetal embryo. As far as is known they give rise to no symptoms.

Lutein Cysts.—If maturation precedes the cyst formation the result will be a lutein cyst. Such a cyst is lined by the characteristic wavy yellow lutein tissue derived from the theca interna. The lutein cells

are loaded with a lipoid which stains red with Scharlach R and is anisotropic when viewed by polarized light. In some cases the inner lining of the cyst may be formed of a single layer of cubical or columnar cells; in others this is absent. The contents may be clear and limpid like those of a follicular cyst, but frequently they are tinged with blood, and a frank hemorrhage is a common occurrence. Sometimes they are jelly-like, probably owing to the coagulation of fibrinogen derived from the blood.

The cysts are usually single, but occasionally they may be multiple. Although frequently much larger than the follicular cysts, they seldom exceed the dimensions of a hen's egg. The presence of multiple cysts, however, may lead to the formation of ovarian tumors of considerable size. Such a condition is often bilateral, and is called a compound lutein cyst. Through the thin walls of these cysts can be seen shining the characteristic yellow lining. These large bilateral cysts are nearly always associated with a recent pregnancy, and frequently with hydatiform mole and chorionepithelioma, conditions to which the excess of lutein tissue may bear some relation. Removal of the mole is often followed by disappearance of the cysts.

Hematoma of the Ovary.—Reference may be made in this place to a blood-cyst or hematoma of the ovary. Theoretically this may be due to hemorrhage into any variety of cyst, but actually the only cyst commonly affected thus is the lutein cyst. The cyst is filled with a blood clot of varying size, and the walls present a flattened lutein lining. Occasionally after dehiscence of a ripe follicle bleeding may continue into a true corpus luteum, with the formation of a hematoma. Large quantities of blood are liable, however, to escape into the peritoneal cavity, and there may be alarming symptoms of internal hemorrhage suggestive of a ruptured tubal pregnancy. Such a hematoma may be distinguished from that arising from a lutein cyst by the thick and wavy character of its yellow lining.

Sampson has called attention to a very interesting type of perforating ovarian cysts with chocolate-colored contents due to old hemorrhage. He has shown that these cysts arise from endometrial tissue in the ovary, an "adenomyoma" of the ovary. The blood which they contain is menstrual blood, and the endometrial tissue in the ovary displays the characteristic changes during the menstrual cycle. These cysts occur during the menstrual life of the patient, usually from thirty to the menopause. They are small in size, as a rule from 2 to 4 c.m. in diameter. The lining of the cavity may be smooth and grey, or rough and brown owing to pigmentation from old hemorrhage.

Evidence of previous perforation can often be seen on the surface of the cyst, and dense adhesions often develop as a result of the rupture. These adhesions are of peculiar interest. At first they were considered to arise from the irritation of the contents of the cyst which had escaped into the abdomen, but it has been shown that they also consist of endometrial tissue, and that they are of the same nature as the well-

recognized adenomyoma of the recto-vaginal septum. Why the escape of the contents of the cyst should lead to this remarkable condition it is difficult to say; but it looks as if there might be some form of implantation spread, similar to that seen in a papillary cyst-adenoma.

TUMORS OF THE OVARY

Tumors of the ovary may be solid or cystic. About 80 per cent are cystic. They are glandular tumors in which the lining epithelium secretes so large an amount of fluid that the gland spaces are dilated

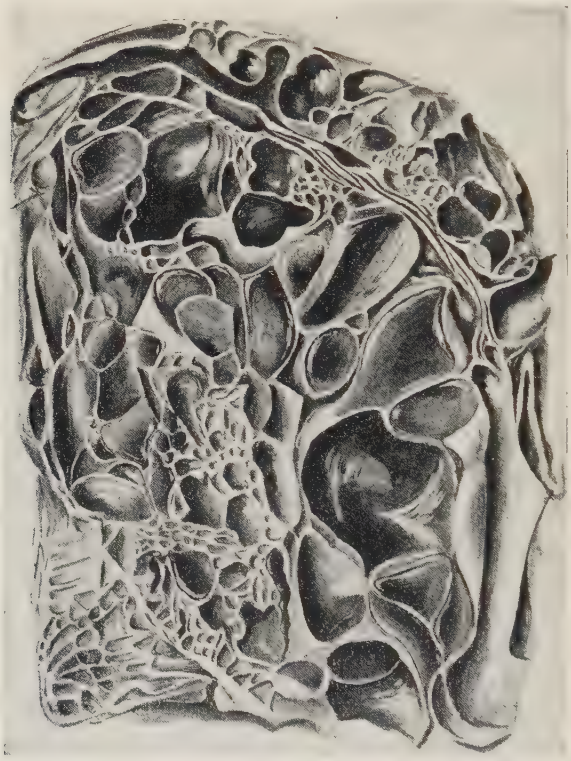

FIG. 195.—Multilocular cyst-adenoma of the ovary. The spaces were filled with thick shiny material.

into cysts. They are therefore called cyst-adenomas. The essential feature of the condition, however, is the epithelial proliferation; it is a tumor before it is a cyst. There are two main forms of cyst-adenoma, which may conveniently be called the multilocular and the papillary varieties.

Multilocular Cyst-adenoma.—This is usually called a cyst-adenoma pseudomucinosum, because the cysts contain a stringy mucoid substance, which, however, is not true mucin, as it does not give the typical reaction with acetic acid, and is therefore known as pseudomucin.

The tumor, which is usually unilateral, may attain enormous dimensions so as to fill the entire abdominal cavity. Nowadays, however, such monstrous growths are rarely seen. The lining epithelium, to whose secretory activity the cysts are due, sends out bud-like projections which are rapidly converted into daughter cysts; these in their turn give rise to granddaughter cysts. A few cysts usually enlarge at the expense of the others, and the walls of the smaller cysts are broken down, remaining as ridges and septa which project into the remaining cavities. There is a well-developed pedicle which is liable to axial rotation, and the tumor does not grow between the

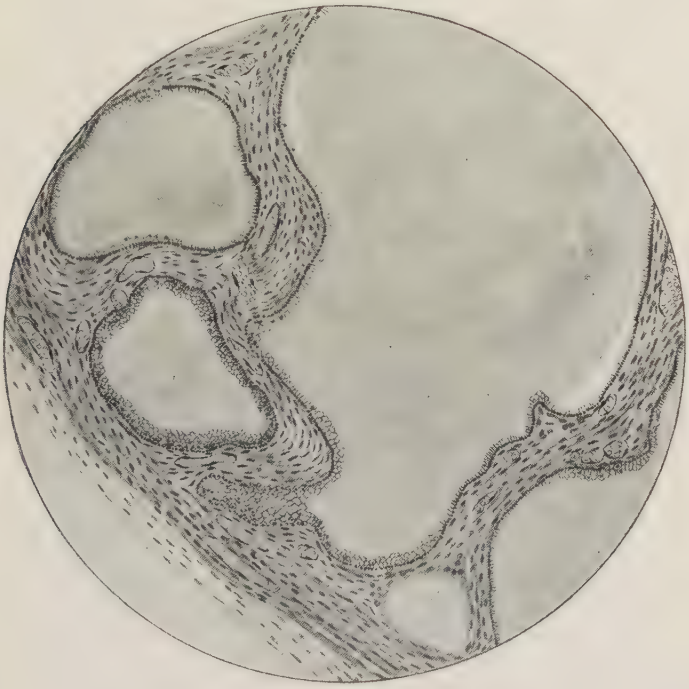

Fig. 196.—Multilocular ovarian cyst-adenoma. The spaces are lined by tall, clear, palisade-like epithelium, with nuclei situated at the base of the cells.

layers of the broad ligament. Unlike subperitoneal fibroids it may form adhesions to the surrounding viscera.

Microscopic Appearance.—The microscopic picture is very characteristic. The cysts are lined by a single layer of tall, palisade, columnar epithelial cells, curiously clear, distended with mucus so that goblet cells are frequently seen, and with small nuclei at the base of the cells arranged in a regular and uniform row. Here and there small spurs of epithelium may project into the lumen of the cyst, but they are not a marked feature as in the papillary variety of cyst-adenoma. The cysts are separated by a small amount of connective tissue.

The *contents* of the cysts consist of a stringy, mucinous material, but varying much in consistence as well as in color, sometimes clear and transparent, sometimes murky and tinged with blood, sometimes greenish and shimmering due to the presence of cholesterin crystals. This material is called pseudomucin.

Pseudomyxoma peritonii is a condition in which the contents of the cysts are discharged into the peritoned cavity, where they form masses of jelly-liked material which act as an irritant, causing fibrous tissue profileration in the peritoneum, so that eventually it may be

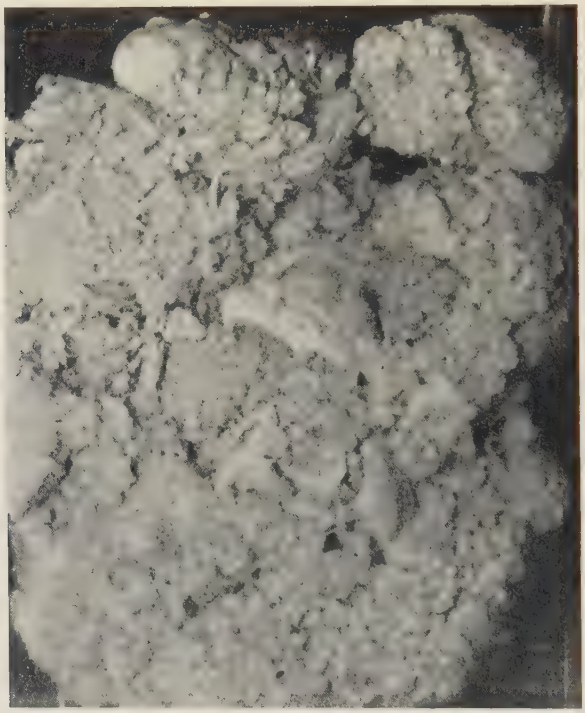

Fig. 197.—Papillary cyst-adenoma of ovary.

impossible to remove the masses. At the same time the epithelial cells of the tumor may become detached and implanted on the peritoneal surface continuing there their secretory activity and thus producing fresh masses of jelly-like material. If the ovarian tumor be examined it will usually be found to present a condition of *pseudomyxoma ovarii;* the cysts are filled with the same clear material, and the lining cells have lost their characteristic appearance and are converted into a degenerated amorphous mass. Although the peritoneal condition cannot be regarded as a malignant one, yet the prognosis is not good, for the masses may continue to grow in spite of repeated

laparotomies, and the chronic peritonitis may eventually lead to the death of the patient.

Papillary Cyst-adenoma.—Although small papillary processes may occasionally be found in the pseudomucinous cysts, it is only in the serous cysts that they attain to any marked degree of development. The cyst-adenoma serosum papillare, as it is called, constitutes about one third of the cystic tumors of the ovary.

These tumors are frequently bilateral but it must be remembered that the two growths may not be of the same age. They may not possess the well-marked pedicle so characteristic of the multilocular cyst, and often they are found growing between the layers of the broad ligament and are therefore difficult to remove. The cyst is usually unilocular but ridge-like projections representing former septa may still persist. The growth is slower than in the pseudomucinous variety, and the tumors never attain to so great a size. The contents are thin, watery, highly albuminous, but contain no pseudomucin. The most important characteristic of the tumor is the papillary processes with which the wall may be studded. They may be scattered diffusely over the entire wall, or may be collected here and there into larger nodules. The processes, in common with the rest of the wall, are covered by a single layer of epithelium, which is low columnar and usually ciliated, thus differing from the epithelium of the multilocular cysts. The processes may be simple in form but occasionally they are highly branched indicating a marked degree of proliferative activity.

Papillary cysts-adenomas have a very distinct tendency toward malignant degeneration; the more branched the processes, the greater does this tendency become. Malignant change is indicated by the soft character of the papillary processes and the irregular disordered arrangement of the epithelium. Even when no malignant anatomical change can be detected, the processes may perforate the wall of the cyst, appear on its outer surface, become disseminated over the surface of the peritoneum, and give rise to rapid and extensive ascites. The percentage of cases which become malignant varies considerably in the statistics of different authorities. For the most part it is about 20 per cent. Erdmann and Spaulding in a recent study of papillary cystadenomas of the ovary claim that in 66 per cent of their cases there were cancerous or precancerous changes. These changes are frequently only to be recognized under the microscope. It is therefore necessary to examine for malignancy every warty or papillary intracystic growth and every secondary cyst however small.

The *prognosis* of the papillary cystadenomas is variable. Even when the condition is undoubtedly malignant the rate of progress is often much less rapid than in other malignant growths. Cases presenting numerous peritoneal metastases have been known to live for 9 and even 12 years. Two of our cases made such an apparently complete recovery after the partial removal of an undoubtedly malignant growth that for a long time doubt was cast on the diagnosis. Eventually the disease nearly always ends fatally when dissemination

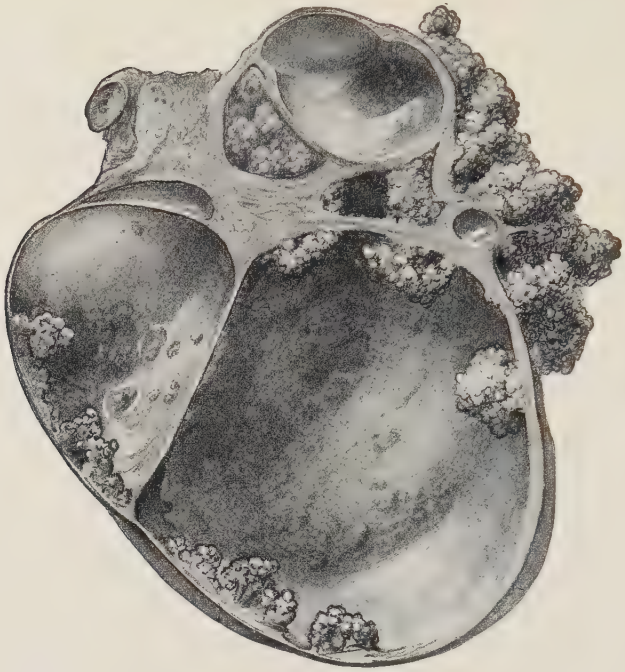

FIG. 198.—Papillary cyst-adenoma of the ovary. The prepillomatous masses have appeared on the outer surface as well as on the inner. (Kelly and Noble.)

FIG. 199.—Papillary cyst-adenoma of the ovary. (Graves.)

of the papillomata has occured, but there are cases on record in which removal of the primary growth has apparently been followed by complete disappearance of the secondary deposits, as shown by a subsequent laparotomy.

In this description of the two great groups of cyst-adenoma of the ovary, the terms multilocular or papillary have been employed for the sake of convenience because they indicate the most striking gross characteristic of the tumor. It must be remembered, however, that the pseudomucinous cyst may develop papillary processes, that the serous cyst may show traces of a multilocular arrangement, and finally that even in a serous cyst no papillary processes may be recognizable by the naked eye. If these exceptions are borne in mind the terms are justifiable and convenient.

The origin of ovarian cyst-adenomas is from the germinal epithelium covering the ovary, which may send downgrowths into the substance of the gland and thus give rise to these cystic tumors. Why in some cases the epithelium should be tall columnar and secrete pseudomucin, why in others it should be low and ciliated and the secretion be serous it is impossible to say.

CARCINOMA

Cancer of the ovary may be primary or secondary. The latter is undoubtedly the commoner, although its secondary nature is frequently overlooked by the clinician.

Primary Carcinoma.—This occurs at the usual cancer period. It is usually bilateral. This does not mean that the growth commences primarily in both ovaries. The second ovary is most probably always infected from the first; the tumors are therefore of very different size.

The *gross appearance* is that of a soft, friable, at times almost brain-like, solid mass, in which cystic spaces are not infrequent. These may be true cysts lined by epithelium, but more often they are merely spaces formed by degeneration of the tumor. Hemorrhagic ascites is a frequent accompaniment.

The *microscopic appearance* is very variable. We may distinguish three main types. (1) The *papillary* form due to malignant change in a papillary cyst-adenoma. (2) An *adenocarcinoma* with the formation of irregular glandular spaces lined by several layers of epithelium; in this form large cystic spaces are common. (3) *Carcinoma simplex*, consisting of solid masses of carcinoma cells separated by a varying amount of stroma.

Metastatic growths are common owing to the tendency of the carcinoma to break through the tunica albuginea of the ovary. The metastases are scattered over the peritoneum and are largely responsible for the characteristic ascites. Secondary growths may be found in the uterine muscle owing to passage of the cells along the Fallopian tubes. The uterus must therefore always be removed along with both ovaries. In such cases it may be difficult or impossible to determine whether the growth originated in the ovary or the uterus.

Secondary Carcinoma.—Post-mortem examination shows that this condition occurs much more frequently than the surgeon suspects. Small metastatic deposits go undetected, as they give rise to no symptoms. On the other hand a large ovarian tumor may claim the surgeon's undivided attention, whereas at autopsy it is found to be secondary to a small silent nodule in the stomach. The growths are almost always bilateral, although one may be considerably larger than the other. The primary growth is most commonly found in the stomach or the large bowel. The uterus is another common source of infection. Although lymphatic spread is possible the cancer cells are usually carried down through the peritoneal cavity and alight

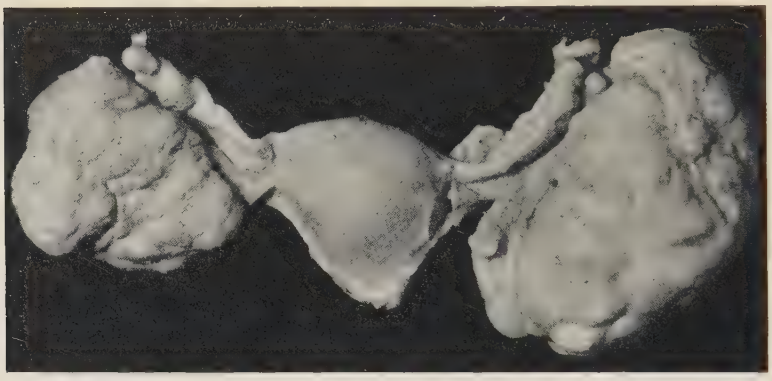

Fig. 200.—Bilateral carcinoma of ovaries secondary to cancer of stomach.

upon the surface of the ovaries, where they set up secondary growths. This mode of spread was beautifully shown in one of our cases where there was a small unsuspected nodule in the stomach, numerous tiny metastatic nodules all the way down the peritoneum, and finally large carcinomatous masses in both ovaries.

The *microscopic appearance* depends upon the nature of the primary growth, and may be that of an adenocarcinoma or carcinoma simplex. In some cases secondary to gastric carcinoma the cells are filled with a clear mucoid material which pushes the nucleus to one side producing a characteristic signet-ring appearance, the so-called Krukenberg tumor.

DERMOID CYST

A dermoid cyst is a form of teratoma, the only form commonly found in the ovary. It constitutes about 10 per cent of all ovarian tumors. In over 10 per cent of cases it is bilateral, and there may even be multiple dermoids in one ovary. It may occur at any age period. It is of slow growth, seldom attains a size larger than a man's fist, and possesses a well marked pedicle which is liable to undergo torsion. It is an innocent tumor, but in rare cases one of the epithelial elements which it contains may undergo malignant change. In a sense it is not

a true dermoid cyst, for such a cyst should be lined by and contain only dermal structures.

The exterior is smooth and glistening, and the yellow color of the contents can often be made out. When removed from the body the wall soon dries and becomes crackly and the contents, which are fluid at body temperature, become semi-solid so that the tumor develops a doughy consistence.

The interior is filled with a yellow, greasy, buttery, material frequently containing long wisps of hair, which may be rolled into balls. The hair is seldom the same color as that on the head of the patient, but with advancing age it is said by Bland-Sutton to turn white and may eventually be shed, so that the tumor actually becomes bald.

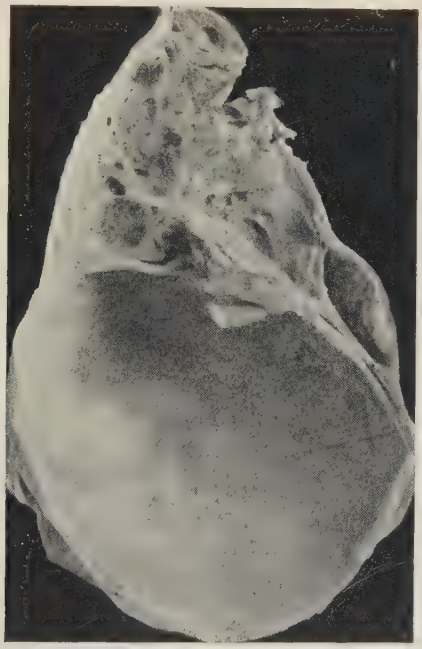

FIG. 201.—Dermoid cyst of the ovary. The solid portion contains normal thyroid tissue.

Many other interesting facts in relation to dermoid cysts of the ovary may be found in Bland-Sutton's treatise on tumors.

The wall is lined by a cubical epithelium. From one part of the wall springs a nipple-shaped mass covered with skin called the dermoid process. This is the essential part of the tumor, as it is from it that the various solid elements are derived. Of these the commonest are skin, hair, and bone, but teeth, cartilage, brain, striated muscle, and many other partially developed structures may occasionally be found. In one case which I examined the principal structure was thyroid tissue, so perfectly formed that it could not be differentiated from a normal

thyroid. In another case there was a small adrenal which contained beautifully formed cortex, and a dark center suggestive of the medulla.

The skin is particularly rich in sebaceous glands, from the secretion of which the contents of the cyst are derived. The cyst, therefore, may be looked upon as a secondary formation due to the distention produced by the gradual accumulation of the secretion of these glands.

Both dermoid cysts and solid ovarian teratomata are supposed to arise not from the original ovum, but from one of the blastomeres formed by primary segmentation of the fertilized ovum becoming separated and included in the ovary. If this blastomere is transported elsewhere a teratoma may arise in that part of the body.

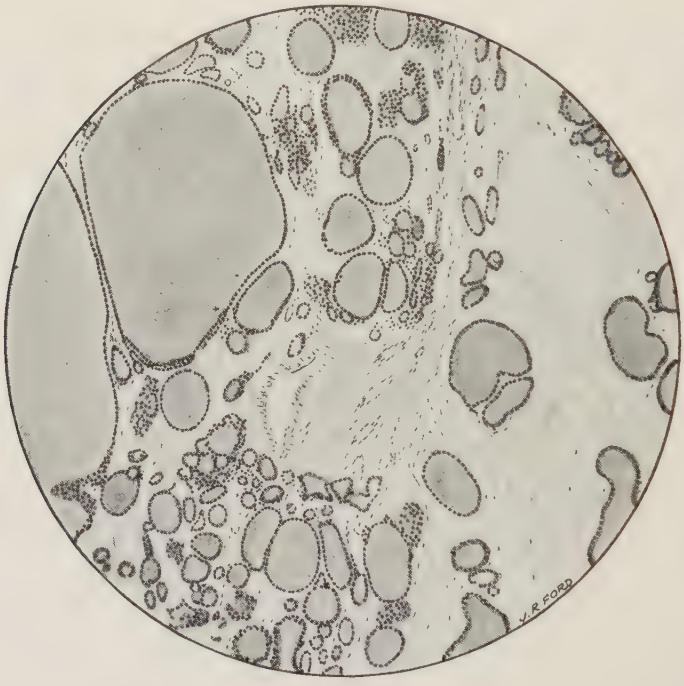

FIG. 202.—Thyroid tissue occurring in a dermoid cyst.

RARE TUMORS OF THE OVARY

Fibroma.—A pure fibroma of the ovary may be circumscribed or diffuse. The former are small, hard, fibrous masses of little clinical importance. The diffuse variety is frequently bilateral and like other solid ovarian growths usually gives rise to marked ascites. They often attain a great size, and the ovary may become as large as a man's head.

Sarcoma.—This is a rare condition. The age period is much earlier than that of carcinoma, and it is not uncommon in children, in whom it is usually bilateral. It may be spindle-celled and of firm consistence,

or round-celled, soft, and brain-like. Metastases are abundant, and ascites, as usual, is an invariable accompaniment.

Endothelioma.—Another rare form of tumor is the endothelioma in which the tumor cells are derived from the endothelium lining the blood vessels or lymphatics, so that dilated spaces are formed lined by endothelium and packed with polymorphic cells. They are usually bilateral, and closely resemble sarcomata in their gross appearance. A perithelioma has been described in which the tumor cells arise from the adventitia of the blood vessels, and form a mantle of cells around the vessels.

FIG. 203.—Parovarian cyst with small papillary processes.

Solid Ovarian Teratomata.—These are very rare tumors. They differ from the teratomatous dermoid cyst in being solid, and in possessing no fully formed structures such as skin and bone. They present a large variety of tissues derived from all three embryonic layers, but all in an extremely rudimentry state of development. They form soft, solid masses, which may attain an enormous size and are usually markedly malignant.

PAROVARIAN CYSTS

The parovarium or organ of Rosenmüller is situated in the mesosalpinx between the ovary and the Fallopian tube, and can be seen when the mesosalpinx is stretched and held up to the light. It consists of a horizontal tube, the duct of Gärtner, which corresponds to the vas deferens in the male, and a series of vertical tubes, homologous with the vasa efferentia and epididymis. These latter are divided into two groups, the outer of which is named Kobelt's tubes.

Cysts arising from the parovarium are of two varieties. The common form consists of small pedunculated cysts no larger than a pea. They are derived from Kobelt's tubes, project from the outer end of the broad ligament, and are of no clinical importance.

The ordinary parovarian cyst arises between the layers of the broad ligament. It never appears before the age of puberty, and may enlarge slowly over a period of years until it attains an enormous size. In other cases, however, it may remain quite small.

The wall of the smaller cysts is thin and transparent, but as the cyst grows larger it may become very thick and tough. The Fallopian tube is stretched over the wall of the cyst and may be greatly elongated. The ovary is attached to the side of the cyst, but in the case of large cysts it may be extremely flattened, incorporated in the cyst wall and difficult to recognize. It may be difficult to differentiate these cysts from a papillary serous cyst-adenoma of the ovary which usually occupies the broad ligament. A parovarian cyst, however, seldom presents papillary processes, and when they are present they are usually in the form of small warts on the surface.

The wall is composed of fibrous and muscular tissue, and is lined by a low columnar ciliated epithelium. It is usually quite smooth. The contents are clear and watery, with a low specific gravity, and a trace of albumen. In large cysts, however, the fluid may be turbid. The condition is essentially innocent.

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CHAPTER XXVII

THE BREAST

Structure.—The breast is a solid glandular organ developed from either the sweat or the sebaceous glands of the epidermis. It is divided into from 12 to 20 lobes of pyramidal shape, each of which may be regarded as a gland in itself. Each is provided with a milk duct opening at the nipple. Smaller ducts branch laterally from the main duct and end in bulbous expansions or alveoli, which at first

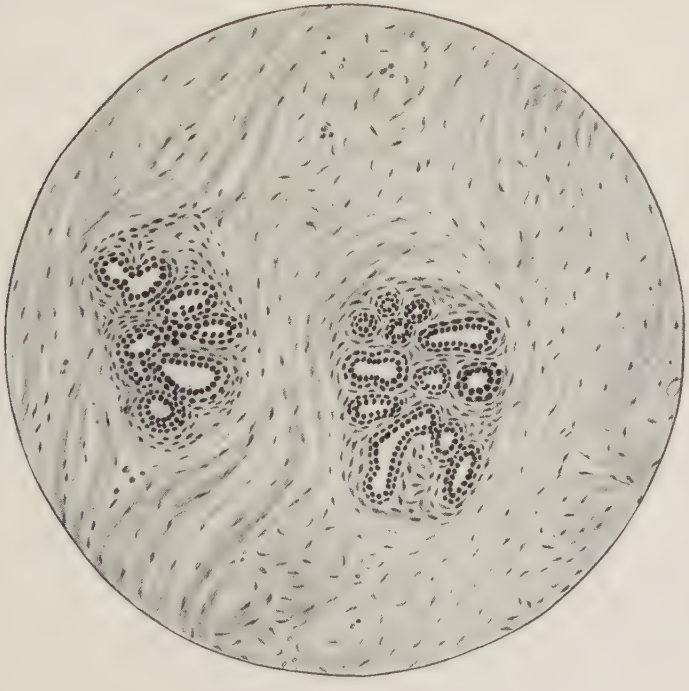

Fig. 204.—Normal breast.

are solid, and only contain a definite lumen during and after lactation. Lobules consisting of clusters of alveoli are thus formed within the main lobes. The number of side ducts and end bulbs increase at puberty, and to a much greater extent during lactation. The cells of the large ducts are columnar, of the small ducts and the acini cubical.

The glandular elements are separated by fibrous tissue and fat. The ducts are surrounded by a loose cellular connective tissue called

the periductal or intralobular tissue. As the terminations of the ducts are approached it surrounds these both individually and collectively, thus grouping them into definite lobules. The intervening stroma consists of dense interlobular connective tissue containing a varying amount of fat.

It must be borne in mind that the histological appearance of the breast varies greatly at different ages. In the young virgin the glandular tissue is scanty and the alveoli have not opened out to form a lumen. During lactation there is such an enormous multiplication of ducts and acini that the fibrous stroma largely disappears, and the entire picture is changed. During later life involution changes occur which will be described presently, and the ducts and acini usually present a double layer of lining cells.

The epithelium lining the commencement of the duct is stratified as far as the ampulla, where it gives place to tall columnar epithelium. When the small ducts are reached the epithelium becomes cubical, and the terminal acini are lined with the same variety. Although at first sight it appears as if the ducts were lined by one layer of epithelial cells, there is in reality a second flattened layer outside, which may be described as a reserve layer for reproducing the lining cells, much as the basal layer of the epidermis replaces the cells lying superficial to it. MacCarty has pointed out the importance of this reserve layer. Its cells proliferate and enlarge in pathological conditions, so that it is common to find the ducts and acini lined by a definite double layer of cells. A single layer can seldom be found in a fibroadenoma, in cystic mastitis the cells are frequently several layers in depth, and in carcinoma they have begun to invade the connective tissue stroma.

The breast has an abundant lymphatic supply. The normal drainage is through the axillary glands of the same side. Many vessels open into the large pectoral plexus, which lies in the pectoral fascia between the posterior surface of the breast and the pectoralis muscle. This plexus is simply a part of the deep fascial lymphatic plexus which pervades the entire body. When the pectoral plexus is invaded by carcinoma cells, therefore, there is no limit to the extent to which they may spread by the process of permeation. One lymphatic trunk passes directly through the pectoralis major and empties into the subclavicular glands without passing by way of the axillary glands. For this reason the subclavicular glands may be enlarged in carcinoma before those in the axilla.

Male Breast.—The male breast is similar in development to that of the female, but remains rudimentary throughout life. The fundamental difference in structure between the male and the female breast is that in the former there are no acini but only a series of ducts of fair size. It is liable to the same disease conditions, but with much less frequency owing to its rudimentary state. At puberty there may be temporary congestion and inflammation. Carcinoma is the most frequent pathological lesion.

Functional Changes.—In the chapter on diseases of the thyroid we have emphasized the fundamental importance of a due regard for the physiological changes to which the gland is so liable if a correct conception of thyroid disease is to be attained. If this be not done it is impossible to understand the apparently disconnected series of morphological pictures which the thyroid may present, and to which an infinite variety of names may be applied. The thyroid is an organ the functional activity of which is subject to great variations in accordance with the stimuli which play upon it, and these functional variations are accompanied by marked variations in structure. The gland may show the hyperplasia of activity, the formation of new acini without evidence of hyperplasia, or the colloid (but not normal) picture of repose after activity. Moreover the epithelial hyperplasia accompanying activity bears a marked resemblance to tumor growth, as is evident from a glance at the microscopic picture of Graves' disease.

These considerations apply with equal force to the breast. There is no organ with so confused a pathology or so bewildering a nomenclature, there is no pathology of which as a student the writer found so difficult to master. The difficulties and roughness of the way will be smoothed, we feel, if the functional variations of the breast together with their corresponding morphological changes be ever kept in mind.

Before the age of puberty the female breast resembles the male in that it possesses ducts but no acini. At puberty the female breast undergoes a great structural change; the ducts commence to branch, and the terminations of the smallest branches expand into acini. Many of these acini are so crowded with cells as to appear quite solid and of course functionless, a condition recalling the structure of the foetal thyroid.

During pregnancy, and still more during lactation, the morphological change is remarkable. The gland becomes the seat of an extreme epithelial hyperplasia, which recalls the hyperplastic thyroid of Graves' disease. The acini are enlarged, large numbers of new acini are formed, the epithelium changes from the cubical to the tall columnar form, and the lumen of the acini may be crowded with fern-like epithelial projections very much like those of thyroid hyperplasia. It is a picture of unbounded epithelial activity, although differing from that of carcinoma in that the activity is restrained and orderly.

Although we have not the same definite knowledge of hyperplasia in the breast as in the thyroid yet there can be no doubt that other stimuli than puberty, pregnancy, and lactation can play upon the breast. The literature contains many examples of the breast showing signs of activity and even lactation in quite young girls. The relation between the condition of the pelvic organs and activity of the breast is undoubted. When both ovaries are removed before puberty the breast fails to develop. Ovulation, or it may be the formation of the corpus luteum, exerts a potent influence on the breast. In many

women there is tenderness and swelling of the breast at each menstrual period, and in some cases actual lactation. The large and active corpus luteum of pregnancy is associated with a high degree of mammary activity, but when ovulation ceases the breast passes into a condition of involution.

For after hyperplasia comes *involution*. As with the thyroid, when the stimulus is withdrawn, activity ceases and the morphological picture changes. Involution is most marked after lactation and at the menopause, the latter being known as senile involution. It also occurs after abortion or pregnancy without lactation. Indeed whenever physiological hyperplasia occurs it will be followed sooner or later by involution.

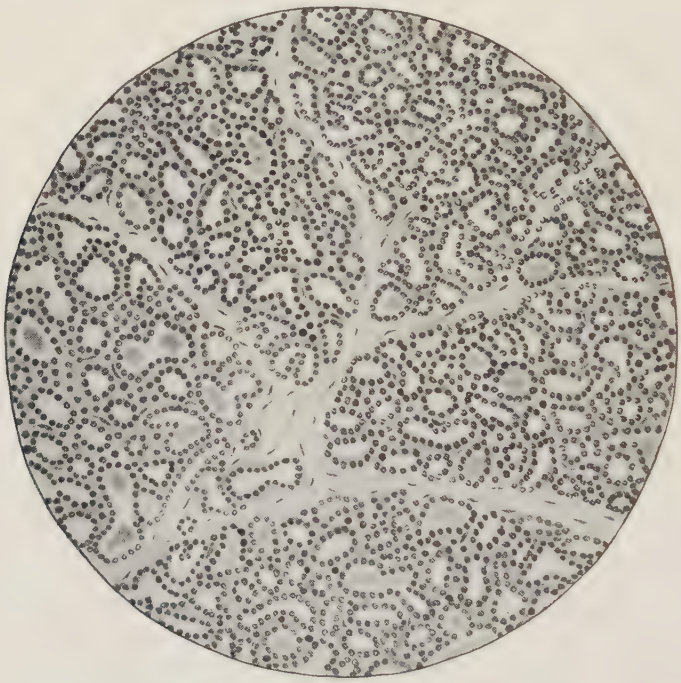

Fig. 205.—Lactating breast, showing the extreme epithelial hyperplasia.

An *involuting breast* is one which varies greatly in appearance in its different parts, for neither evolution nor involution appear to affect the organ in a uniform fashion. The picture is a mixture of atrophy and hyperplasia, and exactly the same mixed picture is seen in a hyperplastic goiter which is passing into the colloid state. Speaking generally there is an atrophy of the parenchyma with an increase in the fibrous tissue. The columnar cells become cubical or flattened. The acini return to their former size and after the menopause disappear altogether. The periductal fibrous tissue may be markedly thickened in the senile breast, and the distinction between interlobular

and intralobular connective tissue is lost, so that the outline of the lobules disappears. Dilatation of the ducts and of some of the acini is common, with the resulting formation of small cysts. It appears probable that this dilatation is not due, as is commonly taught, to obstruction of the ducts from fibrosis, but is rather an initial increase in size at the time when the acinus was enlarging during hyperplasia. Having failed to return to the normal size, and being emptied of its hyperplastic epithelium, it appears as a cyst. Cyst formation, therefore, may be looked on as evidence of hyperplasia followed by involution rather than retention due to obstruction. Round-celled infiltration around the ducts is seen here and there. For this we can give no satisfactory explanation. It has been suggested that retained secretions may act as an irritant and so set up a mild degree of inflammation.

In addition to these changes, which in general are atrophic, there may be signs of hyperplasia. The cells lining the acini and ducts may be two or more layers in depth, or they may fill the lumen. In some cases the evidence of hyperplasia is even more marked. These appearances are usually taken as indicative of the involution process, but it appears more probable that they represent a previous hyperplasia which may not have completely passed off.

So far we have been considering the process of normal involution. There is however a process of *abnormal involution*, or perhaps we should rather say an abnormal hyperplasia-involution process. It may be abnormal in that it occurs at an unusual time—before the menopause or apart from lactation—or it may be abnormal in degree and quality. Still more important, it is probably abnormal in regard to the stimulus which calls it forth. Again the changes are atrophic and hypertrophic. It is the hypertrophic change which is much the more important. The acini proliferate, increase in size, and there is a multiplication of the lining epithelial cells. Cyst formation is common, and papillary masses of epithelium often project into the cysts, giving rise to a tumor-like condition. It may be said that the chief microscopic lesion is epithelial hyperplasia, the chief macroscopic lesion cyst formation.

From this general discussion it will be gathered that the breast, like the thyroid, is an organ liable to fluctuation in functional activity and to corresponding morphological changes; that hyperplasia may completely alter the normal appearance of the gland; that hyperplasia may affect one part of the breast and not another; that when involution follows hyperplasia the picture will be still further complicated; that the breast—again like the thyroid—does not return after hyperplasia and involution to a morphological condition which is perfectly normal; that hyperplasia bears a certain resemblance to tumor formation and may easily be mistaken for it; and that cyst formation (corresponding to the dilated acini of colloid goiter) is to be expected as a result of the hyperplasia-involution process.

The greatest difficulty in studying breast pathology is the nomenclature. A review of the literature on the breast leaves one in a state of absolute bewilderment. Deaver and McFarland in their exhaustive

treatise give 23 names for the condition commonly known as chronic cystic mastitis. A condition such as intracystic papilloma (to give it one of its dozen names) is considered by one author under the heading of neoplasms, by another under that of chronic mastitis. The same used to be true of goiter; every slight variation, often merely dependent on a degeneration, was given a separate name. In both of these cases we are dealing with but one condition, subject it is true to as many variations as a Bach fugue, but with one guiding theme running through them all. Such a conception should make a study of breast pathology a little less confusing.

The common affections of the breast are acute inflammation, chronic mastitis, and tumors. Syphilis is of rare occurrence, and still more rare is tuberculosis.

ACUTE MASTITIS AND MAMMARY ABSCESS

Inflammation of the breast is confined to three periods in the development of the organ: immediately after birth, at puberty, and during lactation. If we exclude conditions of mere congestion which may be almost physiological, and confine the term mastitis to inflammation produced by bacterial invasion, we find that in about 95 per cent of the cases it occurs during the first few weeks of lactation.

The infecting organism is usually the staphylococcus aureus, less commonly the streptococcus. The staphylococcus is more likely to produce a localized, the streptococcus a diffuse inflammation. The organism may enter the breast either through the milk ducts or through cracks in the nipple and thence by way of the lymphatics. The latter is probably the common mode of entry.

The inflammation starts in the interlobular connective tissue, which becomes acutely congested and infiltrated with inflammatory cells, the glandular elements merely showing secondary degeneration. It may involve (1) the subcutaneous tissue in front of the breast, (2) the breast itself, (3) the tissue behind the breast; it may thus be subcutaneous, intra-mammary, or retro-mammary. If pus is formed it will reach the surface with an ease depending upon its depth from the surface. In the retro-mammary form, due usually to extension of infection from the breast into the retro-mammary space, but occasionally secondary to disease of the ribs, the already inflamed breast is pushed bodily forward, as can be seen by comparison with the gland on the other side.

The condition may end in resolution, but frequently goes on to suppuration with the formation of an abscess. The gland is at first congested, hot, painful, and hard, but becomes softer as suppuration develops. Only one segment of the breast may be involved, or the infection may spread into adjoining lobes, so that a series of abscesses may be formed. These may remain distinct, demanding separate incisions for successful evacuation, or there may be a series of intercommunicating cavities with extensive destruction of breast tissue.

The abscess may discharge on the surface, or, more rarely, into the pleural cavity. Healing with fibrosis occurs in one or two weeks in the superficial variety, but in the deeper forms discharging sinuses may persist for several months. Occasionally the abscess may become encapsulated, the pus absorbed, and all that remains is a mass of fatty and calcareous material. Although painful and disabling, the condition is rarely fatal.

The only condition with which acute mastitis may be confused is acute carcinoma. In the latter condition, which usually develops during lactation, there is rapid enlargement of the breast, the skin

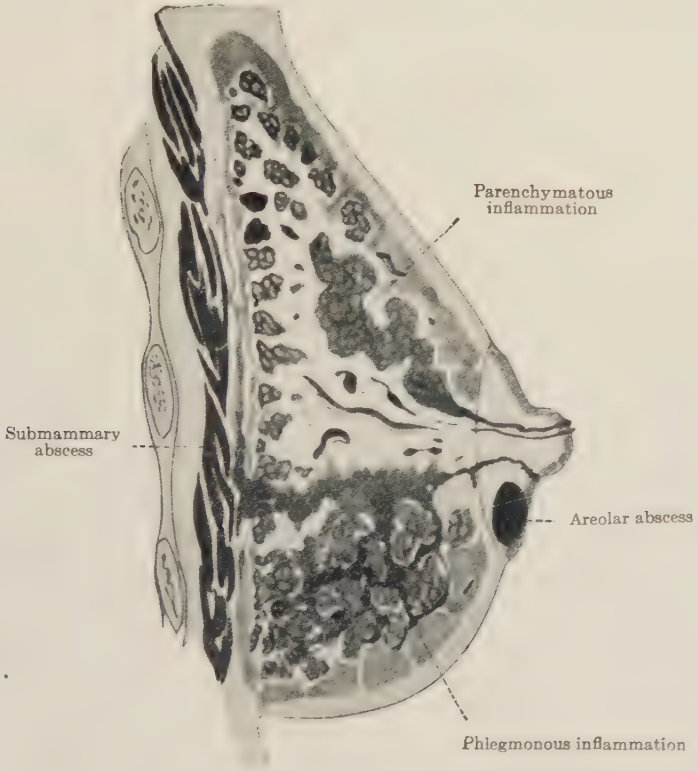

FIG. 206.—Diagram of breast infections. (De Lee.)

is red and inflamed, and there is a considerable degree of fever. The absence of softening, the fixation of the breast, the involvement of the skin, and the marked enlargement of the axillary glands serve to differentiate the two conditions.

CHRONIC MASTITIS

We now approach a subject which is the root and center of all the difficulties in breast pathology. The first problem which we encounter is to decide by which name the condition should be known. Its name

is indeed legion. Amongst the better known are chronic mastitis, chronic cystic mastitis, chronic interstitial mastitis; diffuse fibroadenoma, cystadenoma papilliferum; involution cysts, abnormal involution; cystic disease of the breast, Schimmelbusch's disease. This abbreviated list is given, not with the object of burdening the memory, but that the reader may have some guide when he delves into the literature on the breast.

It is not that the name itself is of such importance, but almost all of these names commit one to a definite theory. The first group suggests that the condition is inflammatory in nature, the second that it is neoplastic, and the third that it is a perversion of involution. The only real evidence in support of the inflammatory hypothesis is the presence of lymphocytic infiltration, and that is always found in involution following lactation and often in senile involution. Nor can we admit that the condition is a neoplasm. There is no tumor—that is a fact from which we cannot get away. It is true that the epithelial hyperplasia may at times suggest a neoplastic process, but the same may be said of the epithelial hyperplasia in goiter. Abnormal involution comes nearest what we want to express, but the fundamental factor is hyperplasia rather than involution. Abnormal hyperplasia would be a preferable term. Cystic disease of the breast has the great advantage of committing one to no theory, but there may be no cysts; although common they are not essential.

As I have no better name to suggest I have deemed it wise to adopt that of chronic mastitis, which is familiar to everyone and useful on that account. It must be clearly understood, however, that the process is in no way inflammatory.

Nature of the Disease.—From what has just been said regarding nomenclature it will be gathered that there is no agreement as to the true nature of the condition. By some it is regarded as inflammatory, by some neoplastic, and by still others as a perversion of involution. In a recent Hunterian Lecture on chronic mastitis Keynes comes to the conclusion that it is not bacterial, toxemic, or traumatic in origin, nor is it related to involution changes in the breast, but that the cause is probably to be found in chemical irritation due to stagnating secretions and epithelial débris. He further points out that the funnel-shaped mouth of a lactiferous duct is lined with an epithelium which normally keratinises on the surface, and that these cornified layers tend to accumulate so as to form an epithelial plug for the duct in the non-lactating breast. These plugs are well seen in longitudinal sections of the nipple, and should the breast awaken into activity the accumulation of secretion in the plugged ducts may give rise to the condition of chronic mastitis.

What we feel to be a more reasonable explanation and one which brings the condition into line with similar conditions in the thyroid and the prostate is arrived at by comparing the account of the physiological changes which the breast undergoes throughout life with that of the lesions in chronic mastitis. As has just been pointed out, the

breast is being continually played on by a variety of stimuli which tend to induce hyperplastic changes followed later by involution. We shall find that the changes characteristic of hyperplasia and of involution may all be duplicated in chronic mastitis: there is evidence of epithelial activity and proliferation in the form of epithelial buds, later atrophy of the epithelium, cyst formation, fibrosis and round cell infiltration—in short, evidence of hyperplasia which may or may not be associated with involution.

Clinical Features.—The patient comes complaining either of pain or a lump in the breast. The pain, although usually slight, may be severe, is often worse at the menstrual period, and frequently neuralgic in nature. One or both breasts may be involved, and there may be more than one lump in one breast. This multiplicity is always strong evidence against cancer. A granular induration is felt when the breast is palpated between the fingers and thumb, much less distinctly when the flat of the hand is used. In this respect it differs from both innocent and malignant tumors. Cysts when present feel hard rather

FIG. 207.—Cystic disease of the breast. It is not often that chronic mastitis shows so many large cysts.

than fluctuating, and give the induration a more coarsely granular character. The induration is frequently confined to one of the sector-like lobes of the breast, whereas in cancer no such restriction is observed. The axillary glands are often enlarged and tender. As in carcinoma they may not be palpable, the condition of the glands should not be used as a means of diagnosis. The cause of the glandular enlargement in chronic mastitis is unknown. Although the disease is commonest at the time of the menopause, it may occur before the thirtieth year. Bloodgood states that it is more frequent in the breast which has never lactated, whether there has been pregnancy or not.

Gross Appearance.—The lesions found in chronic mastitis are so varied that it is difficult to give a comprehensive description of the gross appearance. In a general way it may be said that when incised the indurated area is tough and indiarubbery in consistence, yellowish-white in color, not encapsulated, and not definitely circumscribed.

It has not the stony hardness of a scirrhous carcinoma, nor does it present the familiar yellow streaks and specks so characteristic of that condition. Pink and grey dots of new-formed glandular tissue may be slightly raised above the surrounding surface. Cysts of varying size and number are usually present, although sometimes so small as to require most careful inspection. In some cases the whole area may be converted into a series of cysts; this is the classical cystic disease of the breast. Papillomatous processes may project from the walls of the larger cysts.

The best recent detailed study of chronic mastitis is that of Bloodgood, who in a masterly paper reviews 350 cases of the disease from the clinical and from the pathological standpoints. He gives an excellent description of the various forms which the disease may take, but the different varieties are considered almost as separate entities, and no underlying fundamental principle can be traced throughout the series. The paper is of particular value in that the clinical history of the patients has been followed, in some cases for as long as 29 years.

In the 350 cases Bloodgood found 210 with large cysts, either single or multiple, and 140 without large cysts.

By far the commonest type of large cyst is what Bloodgood calls the blue-domed cyst. The blue dome of the cyst is usually seen after dividing the subcutaneous fat, but sometimes a zone of breast tissue has to be divided also. When the cyst wall is nicked the blue color disappears. The contents of the cyst are clear or cloudy, never hemorrhagic. Hemorrhage into a cyst indicates carcinoma. The wall is smooth; there are no papillomata. There were 174 examples of single large cyst.

Of multiple large cysts in one or both breasts there were 28 cases. These cysts also are of the blue-domed variety. This is the classical cystic disease of the breast. The gland is riddled with large cysts of the same character as that just described.

In 8 cases the cyst resembled a galactocele, although none of the cases had any relation to lactation. This cyst is white-domed, contains a milky fluid, and the contents coagulate when alcohol or formalin are added.

In the remainder of Bloodgood's cases there were no large cysts. Further details will not be given, for his nomenclature is not in line with the general principles which have been laid down. He speaks, for instance, of nonencapsulated adenomatous areas and nonencapsulated cystic adenoma. These terms are undesirable in the discussion of a condition which he himself calls chronic cystic mastitis.

One last condition may be mentioned. In one form of the disease some portion of the breast or it may be the entire breast is filled with minute cysts and dilated ducts. This is the form to which the name Schimmelbusch's disease was originally applied.

Microscopic Appearance.—It is the extremely varied microscopic picture which has given rise to so many conflicting opinions regarding chronic mastitis. Considered individually the different features are

largely meaningless, but when regarded as parts of one process of epithelial hyperplasia or retrogression they become more intelligible. The principal changes are as follows.

1. *A formation of epithelial buds* similar to those seen during the evolution of the breast at puberty. Each bud consists of a solid mass of cells, and on account of its compact nature it stains very darkly. Such a condition may be compared with the fetal adenoma of the thyroid. The parenchyma of the breast seems to be increased, and the appearance is described by some writers as adenomatous.

2. *Cyst formation* is extremely common. In addition to the larger cysts easily seen by the naked eye there are numerous tiny cysts less than a millimeter in diameter. The recent work of Lenthal Cheatle

Fig. 208.—Cystic mastitis. Marked epithelial hyperplasia, cyst formation, and fibrosis.

on the formation of cysts in the breast deserves careful study. He has come to the conclusion that the majority of cysts are formed not from the acini but from the ducts.

3. *Papillary formation* is a characteristic change in many cases, as might be expected from our preliminary considerations. It corresponds to the adenocystic change of Bloodgood and the secondary epithelial hyperplasia of MacCarty. At first the epithelial cells merely multiply and become heaped up in the dilated space, but presently they begin to send finger-like processes inwards. These fuse

together in places so as to form a mass in which there are many spaces, an appearance described by some authors as adenomatous. The interlacing processes may form a beautiful filigree pattern which Lenthal Cheatle describes as laciform or sometimes resembling a cart-wheel. The microscopic picture of epithelial hyperplasia may closely resemble that of exophthalmic goiter or hyperplasia of the prostate.

4. *Pale epithelial cells*, the "blasse Epithelzellen" of the Germans, form a peculiar finding occasionally seen in this condition. The cells are large and clear, with abundant cytoplasm and a vesicular nucleus. Small cystic spaces are filled with these cells, which are desquamated from the lining membrane. They become softened and liquefied, and form the fluid contents of the cysts in Schimmelbusch's disease.

5. *Atrophy of the epithelium* rather than hyperplasia may be the dominant factor. The cells lining the acinus become more and more indistinct, until finally the acinus itself is unrecognizable. As in the case of hyperplasia, the atrophy is not uniform; it may be present in some lobules but not in others.

6. *The connective tissue* undergoes changes as well as the parenchyma, but they are probably not primary in nature. As a rule there is a marked increase. This is best observed in the periductal fibrous tissue, which may be so dense as to suggest a periductal fibroma. Round-celled infiltration around the ducts is fairly common, especially in those ducts which contain much secretion. This appearance has been taken to indicate that the condition is inflammatory, and is probably responsible for the term chronic mastitis.

The Relation of Chronic Mastitis to Carcinoma.—At the present day there is no question more interesting and more vitally important in breast pathology than the relationship of chronic mastitis to carcinoma. It is interesting because opinions vary so enormously. It is important because the surgeon has to decide whether or not he will perform a mutilating operation to safeguard his patient against the future possibility of cancer.

The modern tendency is to regard cystic mastitis as a dangerous and precancerous condition, and some surgeons treat any cystic condition in the breast in the most radical manner lest a worse thing should befall their patient. Such an attitude is entirely indiscriminating, and reduces the surgeon to the level of a mere operator. A mutilating operation should not be performed unless there is very good reason for it.

It has never been proved pathologically that chronic mastitis can become converted into a carcinomatous process. The epithelial hyperplasia is no more malignant than is the hyperplasia of goiter, although both bear some resemblance to a neoplastic process. The fact that the two are not infrequently combined counts for nothing. Chronic mastitis in some degree is so common that it would be remarkable if it were not occasionally associated with carcinoma. Moreover even if carcinoma and chronic mastitis are associated, what proof is there that the former is caused by the latter? It is more

probable that the opposite is the case. Chronic mastitis is associated with such breast lesions as fibroadenoma, gumma, tuberculosis, etc., where it is certainly an effect rather than a cause. The same is most probably true of carcinoma also.

It must be admitted that such distinguished observers as Ewing and Sir Lenthal Cheatle are strongly in favor of the view that chronic mastitis is a precancerous condition. In this respect, however, the only really satisfactory evidence is that provided by clinical results over a long period of time and correlated with pathological findings. From this viewpoint there is no work so satisfactory as that embodied in Bloodgood's recent paper to which reference has already been made.

Here we have a series of 350 cases of chronic mastitis, treated in many instances by conservative removal of only the part involved, and with subsequent histories extending in some cases for 29 years. "Among the 350 cases of chronic cystic mastitis of the various types here described we have had an opportunity to study the entire breast in 222 cases in which it was removed. In not a single instance have we found gross or microscopic cancer. The same is true of about 600 benign breast lesions other than those discussed here. Many of these breasts were unnecessarily removed." "The development of cancer in the breast after the removal of a zone of breast the seat of chronic cystic mastitis is apparently not more frequent than the normal incidence of cancer in the same number of women at the same age who had not been operated on: three out of 128 cases—about 2 per cent." "My conclusions are that chronic cystic mastitis is not a lesion of the breast which at the present may be considered precancerous, and its presence does not demand either the complete excision of the breast, or the complete operation for cancer."

TUMORS OF THE BREAST

Of the true tumors of the breast, 95 per cent fall into two groups, fibroadenoma and carcinoma. The former constitute about 15 per cent, the latter 80 per cent. Every tumor of the breast should be regarded as malignant until it has been proven to be innocent, and the only way to make certain is to make an exploratory incision and judge either from the gross or from the microscopic appearance. An early carcinoma may so resemble a fibroadenoma clinically as to deceive the very elect.

Fibro-epithelial Tumors

The innocent tumors of the breast are essentially fibro-epithelial overgrowths which are limited by a capsule. Sometimes the fibrous element is predominant, sometimes the epithelial. The development of cysts will materially modify the character of the tumor.

As a matter of fact it is really difficult to draw a hard and fast line between some cases of chronic mastitis and fibro-epithelial tumors. To the naked eye the capsule is a satisfactory distinguishing feature, but the microscopic picture may be very similar in the two conditions.

Three main varieties of fibro-epithelial tumor may be recognized: (1) pericanalicular fibroadenoma, (2) intracanalicular fibroadenoma, and (3) duct papilloma.

1. **Pericanalicular Fibroadenoma.**—This is sometimes called the hard fibroadenoma of the breast. Rarely attaining a great size it is well encapsulated by a definite sheath of dense fibrous tissue from which it pops out when the sheath is incised. Often, however, it is attached to the sheath at one point. Its most notable clinical charac-

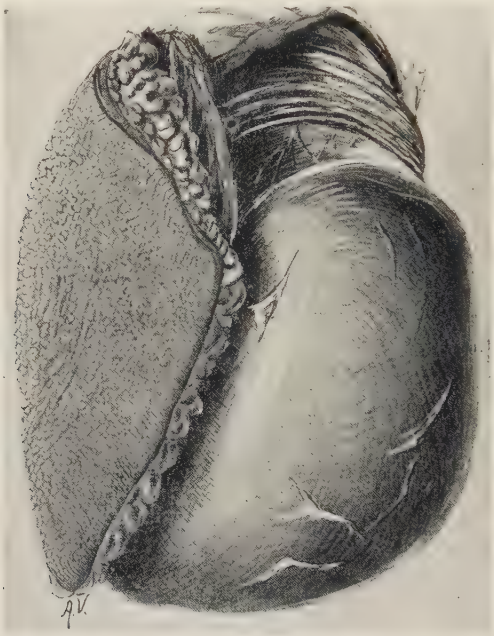

FIG. 209.—Fibroadenoma of the breast. The encapsulated character of the growth is well shown.

teristic is its mobility. So slippery may it be under the hand as to be quite difficult to grasp.

On section it is whitish in color, slightly granular, and displays a number of surface markings or splits. It is very firm, but cuts like cartilage and not with the gritty sensation felt in a scirrhous carcinoma. During lactation the fibroadenoma shares with the rest of the breast in the general hyperplasia.

Microscopically the tumor consists of an overgrowth of both fibrous and epithelial structures. The acini and the ducts appear more numerous than normal, and are surrounded by a stroma of fibrous tissue which varies greatly in density, and which is most marked around the ducts; hence the name periductal or pericanalicular. Although resembling the structure of the normal breast, that structure is never perfectly repeated. The glandular arrangement is more diffuse, and new lobules are not formed.

2. Intracanalicular Fibroadenoma.—This is the common variety of fibroadenoma. It is more of a fibroma than an adenoma. When small it has a moist and succulent appearance which may suggest a medullary carcinoma, but the lack of encapsulation of the latter serves to differentiate it. When larger the cut surface may resemble the hypertrophied prostate, and give the appearance as if many small cauliflower-like masses were enclosed in cysts. These little papillomata can indeed be turned out, but they are found to be attached by a pedicle.

Microscopically there is a remarkable proliferation of connective tissue which projects into the ducts in the form of polypoid masses,

Fig. 210.—Intracanalicular fibroadenoma of the breast. Masses of proliferated fibrous tissue project into the dilated ducts.

producing great elongation and distortion of the ducts, which are usually much dilated. The section often does not pass through the pedicle of these polypoid masses, with the result that the dilated duct appears to be crowded with masses of fibrous tissue, each covered by a layer of epithelium invaginated from the duct wall, and separated from one another by a series of branching slits. The connective tissue is so loose in texture that some writers call the condition a myxoma.

These tumors may occasionally attain to a great size, and the larger varieties are said to be liable to sarcomatous transformation.

3. **Duct Papilloma.**—This condition, which bears a certain resemblance to that which has just been described, has had a bewildering variety of names attached to it. Adeno-cystoma, intracanalicular cystadenoma, papillary cystoma, proliferous cyst, villous papilloma, and intracystic papilloma are among the names worth mentioning, for they convey some conception of the nature of the condition.

Fig. 211.—Breast. Duct papilloma.

The gross appearance varies considerably. In its simplest form the tumor appears as a little papillomatous growth which projects into a dilated duct usually close to the nipple. Whether the dilatation precedes the papilloma or the papilloma the dilatation appears to be as difficult a problem to solve as that of the order of precedence in the case of the hen and the egg. More rarely the papilloma projects into a preformed cyst, in which case it should be called a cyst papilloma.

At first the nodule consists of a series of epithelial folds, and in its early stages has the appearance of a minute raspberry. As growth proceeds the tumor becomes arborescent or dendritic. The dendrons or villi usually adhere together fairly well, so that the surface appears velvety rather than villous. The larger specimens distend the duct and become a solid compact mass, although in reality composed of interdigitating papillary processes.

Microscopically the picture is again a varying one. The early stage will show a typical papillary or villous formation, the delicate stroma being covered by a single layer of columnar epithelium. The larger specimens appear to have an adenomatous structure owing to the gland-like spaces formed by the interlacing processes. It is on this account that such misleading terms as adeno-cystoma and cystic adenoma have been applied to the condition. The blood vessels are large and thin-walled, so that hemorrhage is common, and a discharge from the nipple, either blood-stained or serous, is one of the most characteristic symptoms.

It will be observed that although there is a superficial resemblance between duct papilloma and intracanalicular fibroadenoma there is this essential difference; in the former the actively growing element is epithelium, whilst in the latter it is fibrous tissue.

There appears to be a definite relation between duct papilloma and duct carcinoma (page 559); the latter is a condition of only local malignancy.

CARCINOMA

The breast shares with the uterus the distinction of being the commonest site for carcinoma. About 40 per cent of all carcinomas occur in this gland. It is a disease of the involuting breast, being commonest at the time of the menopause, and rare before the age of thirty-five. It may, however, be met with at any time after the twentieth year, and some slow forms may last for five, ten, or even fifteen years. Spontaneous recovery has been known to occur even after widespread secondary growths have been set up.

As is natural in a complex organ like the breast, the tumor presents marked variations in physical appearance, rapidity of growth, and histological arrangement. As a consequence a great number of names have been applied to the different varieties. Deaver and McFarland give a list of 54 names which they have found in the literature. In general terms we may say that the carcinoma may be spheroidal-celled or columnar-celled. The former arises from the epithelium of the acini and is a carcinoma simplex, the latter arises from the epithelium of the ducts and is an adenocarcinoma.

We have seen that in fibroadenoma the proportion of connective to epithelial tissue may vary markedly, giving rise to corresponding variations in the physical character of the tumor. The same is true for carcinoma. The fibrous tissue is often so abundant that the epithelial hyperplasia appears almost secondary. Such growths are called hard or scirrhous carcinomas. Or the tumor may be highly cellular with comparatively scanty stroma. This is a soft, encephaloid, or medullary cancer. When the epithelial cells are arranged in tubular fashion an adenocarcinoma results. Colloid degeneration may occur in any of the forms, giving rise to colloid cancer.

The *etiology* of cancer of the breast is unknown. Two factors are often mentioned, trauma and chronic mastitis. There is no proof that trauma bears any etiological relationship to cancer of the breast. It is true that a history of a blow may frequently be obtained, but the breast is a superficial organ which must receive countless blows of which we hear no more. If trauma is a factor to be considered it is likely that the blows are physiological rather than physical.

Nor can it be said that the relationship of chronic mastitis to carcinoma has been set on a firm basis. It is true that as cancer does not develop in healthy tissue a condition of chronic mastitis may lay the breast open to attack. Further than this we cannot go. The question has already been discussed on page 540.

As the scirrhous form of carcinoma is by far the most common and important, the general characteristics of cancer of the breast will be considered with reference to this variety.

Scirrhous Carcinoma.—*Clinical Features.*—A scirrhus begins as a hard nodule which can best be appreciated with the flat of the hand. The commonest site is the upper and outer quadrant, but it may commence in any part of the breast. It is not confined to one lobe, but extends in an irregular manner. It becomes fixed to the deep fascia and later to the skin. There may be local flattening or general shrinkage of the breast. The skin may become ulcerated, so that the tumor projects on the surface as a fungating mass. Slight dimpling of the skin due to lymphatic edema occurs at an early stage. Involvement

Fig. 212.—Fungating carcinoma of the breast.

of the large milk ducts is responsible for fixation and later actual indrawing of the nipple. Although more slowly growing than the medullary form the end results are worse instead of better. The axillary, subclavian, and supraclavicular glands may be enlarged and hard, but neither painful nor tender. It cannot be too strongly emphasized that glandular enlargement is not characteristic of the early and operable stage of the disease, and its absence should never be accepted as a sign of diagnostic value. *Most of the classical symptoms such as fixation to the deep fascia and retraction of the nipple are late*

signs due to the fibrosis which accompanies the epithelial overgrowth. and are therefore not present in the early stages.

Spread.—A knowledge of the methods of spread is essential to the surgeon, because no operation is of avail unless it removes not only the primary growth but the whole infected area. It used to be thought that the main factor in dissemination was embolism either by the lymphatics or the blood stream. The researches of Sampson Handley have shown that this is not the case. He has demonstrated that carcinoma of the breast should be regarded not so much as a tumor of an organ as an invasion of the lymphatic system commencing at the primary growth and spreading outwards in a constantly enlarging circle which has no respect for anatomical boundaries. Embolism by the lymph stream is responsible for the early infection of the neighboring lymphatic glands, and in the very late stages metastases in the brain and other distant viscera as well as general skeletal involvement may be attributed to spread by the blood stream, but there can

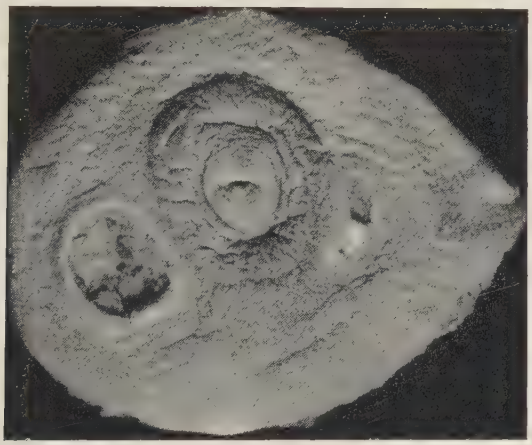

FIG. 213.—Malignant ulcers of breast from underlying carcinoma.

be no doubt that the appearances which one observes both in surgical specimens and on the autopsy table are best explained by the results of Sampson Handley's painstaking histological work on the spread of cancer by lymphatic permeation. Carcinoma of the breast may be disseminated in five ways: (1) infiltration, (2) permeation, (3) transcelomic implantation, (4) lymphatic embolism, and (5) blood embolism.

1. *Infiltration.*—The cancer cells extend outwards from the primary growth, and infiltrate the tissue interspaces between the fat-cells and bundles of fibrous tissue. These interspaces may be regarded as lymph spaces, but they are not lined by endothelium, and the cells do not enter the lymph vessels. The process of infiltration, although earliest in point of time, is slow, only affects the primary tumor nodule, and is of relatively little importance as a means of general

dissemination. The familiar appearance of cancer cells arranged in columns in single file is an indication of the infiltration of tissue spaces.

2. *Permeation.*—When the cancer cells enter a lymphatic vessel they commence to grow along it, even "up-hill" in a direction contrary to the lymph flow. This process Handley has called lymphatic permeation, and he has shown by microscopic examination of long strips

Fig. 214.—Carcinoma of breast showing indrawing of nipple and condition of pig-skin.

radiating from the primary nodule that it is by far the most important method of spread, a method which is effective not only within the lymphatic area where the primary nodule is situated but also as a means of general dissemination.

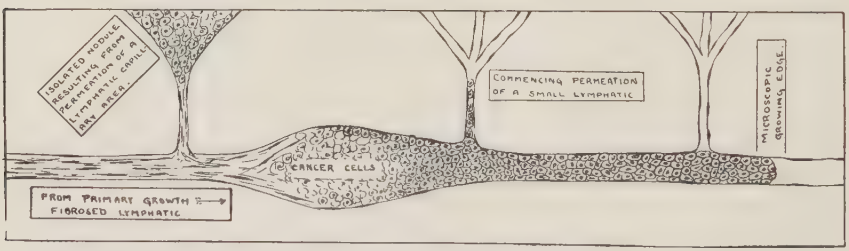
ISOLATED NODULE RESULTING FROM PERMEATION OF A LYMPHATIC CAPILL ARY AREA.
COMMENCING PERMEATION OF A SMALL LYMPHATIC
MICROSCOPIC GROWING EDGE
CANCER CELLS
FROM PRIMARY GROWTH
FIBROSED LYMPHATIC

Fig. 215.—Diagram illustrating the permeation of a lymphatic of the breast by carcinoma cells, and showing the distension of the lymphatic, the formation of a skin nodule, and the lymphatic fibrosis. (After Sampson Handley.)

The cancer cells grow downward in the fine lymphatics until they reach the plexus of lymphatics which lies upon the deep fascia separating the subcutaneous fat from the pectoral muscles, and it is along the plexus of the deep fascia and the muscular aponeuroses that the principal spread takes place. The cells grow steadily outwards in a centrifugal fashion, meeting with but little resistance, and forming

a circle of ever-widening radius, of which the center is the primary focus.

This circle is in no sense a solid mass of tumor tissue. As the ripple of permeation spreads outward the cells distend and burst the lymphatics, those in the center of the mass degenerate, and the degenerated cells call forth a connective tissue reaction such as is described on page 162. The resulting round-celled infiltration and perilymphatic fibrosis obliterate the vessel and destroy most of the epithelial cells, although a few are left here and there to set up secondary nodules. This healing process fails to overtake the actual growing edge, itself only a few millimeters in width, and the round-celled infiltration is never seen among the cells at this edge which is the most important part of the tumor, and the one against which treatment, both operative and radiological, must be directed. The circle of extension may finally attain a diameter of two feet, involving the cranium above, the vertebral column behind, and the groin below.

Nodules may appear in the skin, particularly after operative removal of the tumor. In some cases these may be attributed to lymphatic spread along the skin and subcutaneous tissue, but they are usually

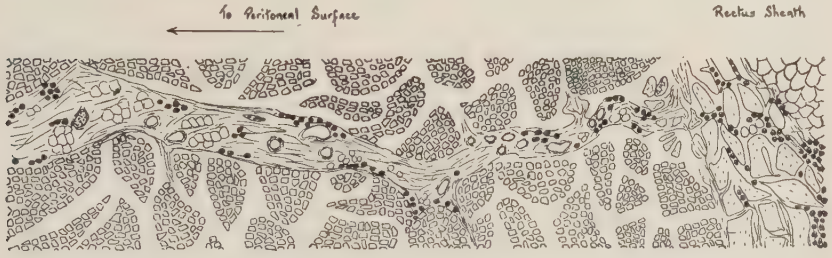

FIG. 216.—Epigastric invasion from carcinoma of breast. The carcinoma cells are passing from the rectus sheath through the muscle toward the peritoneum. (After Sampson Handley.)

to be explained by infection from the fascial plexus. The lymphatics of the skin begin in the dermal papillæ as blind end-sacs, extend downwards at right angles to the surface through the deeper layers of the dermis and the underlying subcutaneous fat and discharge into the lymphatic plexus which lies on the deep fascia. The cancer which spreads along the deep fascia may thus grow up along some of these lymphatics, and here and there blossom out into skin nodules. The obliteration of the deep lymphatics by the defense fibrosis may give rise to *lymphatic edema* of the skin. There is swelling of the corresponding area of skin, but those points which are anchored by the hair follicles are unable to participate in the general expansion, so that numerous little dimples are formed, giving an appearance not unlike that of the skin of an orange, the condition known as "pig-skin" or "peau d'orange." Obstruction of the larger lymphatic vessels of the arm may cause a brawny swelling and induration similar both in appearance and causation to that of elephantiasis.

The skin nodules may be local or may be widespread in their distribution. In exceptional cases they have extended as far up as the scalp and as far down as the groin. They are never found in the arms below the middle of the humerus and in the legs below the upper third of the femur. It is of interest to note that the bones commonly the seat of secondary growths lie within the area liable to subcutaneous nodules. Indeed the nearer a bone is to the primary growth the more frequently is it the seat of secondary growths. The sternum and ribs are most often affected, then come the spine, the upper end of the humerus, the upper end of the femur, and the cranial bones. The clavicle seems to be an exception to the general rule. The bones distal to the elbow and knee are very rarely involved.

In the course of extension by permeation the carcinoma cells may invade the body cavities, both pleural and peritoneal. The pleural

Fig. 217.—Epigastric invasion. Carcinoma cells penetrating the linea alba and reaching the subperitoneal fat. (After Sampson Handley.)

cavity may be invaded along lymphatics which pierce the pectoral and intercostal muscles and communicate with the subpleural lymphatics. The peritoneal cavity is invaded from the abdominal wall. Stiles has shown that the lower and inner margin of the breast is only one inch from the interspace between the eusiform cartilage and the seventh costal cartilage. In this region the lymphatic plexus in the epigastric aponeurosis is only separated from the subperitoneal lymphatics by the linea alba, so that when the cancer cells have extended one inch beyond the breast they have merely to pass through a single layer of fibrous tissue traversed by lymphatics. It is not surprising, therefore, that through this weak spot cancer frequently reaches the peritoneum even before it has succeeded in penetrating the pleura.

3. *Trans-celomic Implantation.*—Numerous fine anastomoses connect the lymphatic plexuses of the deep fascia with the subendothelial plexuses of the pleura and peritoneum. The cancer cells, having reached the latter plexuses, burst the lymphatics, escape into the serous cavities, and are distributed throughout these cavities by gravity and by visceral movement. They become implanted at various points on the serous surface of the viscera, where they set up secondary growths, with a resulting embolic infection of the glands which drain that area. Gravity plays a part in this dissemination, so that the diaphragm and the pelvic viscera, particularly the ovaries, are often the seat of metastases. Invasion of the abdomen without corresponding invasion of the thorax occurs in about 15 per cent of cases. If embolism by the blood stream was responsible for the metastases the cancer cells would all require to pass through the lungs first before reaching the abdominal viscera.

The lung may be infected by permeation from the bronchial glands. I recently had the opportunity of studying a striking example of late permeation of the lung. The patient, a girl at that time only 21 years of age, had a carcinoma of the breast removed; the diagnosis was verified by the microscope. Five years later she developed pulmonary symptoms and died after an illness of a few months. At the autopsy there was no evidence of local recurrence. In the center of the lung near the hilus there was a carcinomatous mass, and a considerable area of the surrounding lung was indurated, although showing no gross evidence of nodules. The bronchial glands were the seat of metastases. Under the microscope the indurated portion showed a beautiful picture of peribronchial lymphatic permeation, each bronchiole being surrounded by a mantle of carcinoma cells similar in appearance to those of the central mass.

The liver is involved far more frequently than any other abdominal organ. Its method of infection is interesting. Cancer cells entering the peritoneal cavity may be implanted directly on the surface of the organ. Such a method would hardly explain the frequent occurrence of nodules scattered throughout the substance of the liver. The usual route appears to be along the lymphatics of the falciform ligament to the portal glands, whence the disease permeates the lymphatics of the portal tracts and sets up secondary growths throughout the liver.

Cancer, like empyema, apparently has great difficulty in penetrating the diaphragm from above downwards, possibly on account of the strong lymph current which flows in the reverse direction. The crural lymphatics, however, unlike those of the rest of the diaphragm, drain into the lumbar glands instead of those of the thorax. In this way retro-peritoneal infection may occur, with the formation of metastases in the kidney, the adrenal, and the lumbar vertebræ.

4. *Lymphatic Embolism.*—Cancer cells entering one of the larger lymphatic vessels are carried as emboli to the glands which drain the area. The axillary glands are those most frequently involved. Then come the subclavian glands. Here they may grow and form secondary

deposits. This form of extension occurs early in the disease. The emboli may originate not only in the primary mass but also in the secondary nodules which are the result of permeation in the abdomen and elsewhere. Recurrence after the operative removal of breast carcinoma in cases where the deep fascia has been extensively removed as recommended by Handley occurs more frequently in the anterior mediastinal and supraclavicular glands than elsewhere. Those of the carcinoma cells which succeed in passing the barrier of the lymph

Fig. 218.—Disseminating carcinoma of breast. Extensive invasion of skin reaching line of incision on both sides. Miliary carcinoma of pectoral muscle. (Ewing.)

glands and enter the blood stream are usually destroyed. The glands thus act as a fairly efficient barrier to further spread.

5. *Spread by the Blood Stream.*—There can be no doubt that carcinoma of the breast may be disseminated by the blood stream. The only difficulty is to know how frequently this method is employed. Apparently it seldom occurs until the late stages of the disease. The malignant cells do not find a suitable pabulum in the rich blood plasma,

and although emboli may be observed in the capillaries of the lungs and other organs the cells are usually in a state of degeneration.

The brain and other distant organs may be infected through the blood. In the brain the metastases are most frequently found in the lateral lobes of the cerebellum. Although in ordinary cases secondary growths in bone are due to permeation, as is evidenced by the distribution of the metastases, yet there is sometimes so general and widespread a dissemination that embolism by the blood stream seems to be the only reasonable explanation. In one case which came under my

FIG. 219.—Carcinomatous ulcer of breast.

notice almost every bone in the body, as shown by the X-rays, was involved, and there were several spontaneous fractures. The strangest feature of the case was that just when arrangements had been made to admit the patient into a home for incurables the fractures began to unite, and all the secondary growths disappeared. Such cases are not unknown, and their subsequent history is usually that of the present case—recurrence in the internal organs after a varying interval of time with a rapid exitus of the patient.

Gross Appearance of Scirrhous Carcinoma.—The breast is small, hard, and flattened. The tumor is firmly adherent to the surrounding tissue, and sends radiating processes out into the fat. When incised it cuts with the peculiar gritty sensation of an unripe pear, and often presents the white striations seen in that fruit, these being bands of fibrous tissue. The cut surface is of a greyish color, contrasting with the dense white of a fibroadenoma and the yellow tinge of cystic

Fig. 220.—Scirrhous carcinoma of breast. The main tumor is situated below a much indrawn nipple. There are several smaller outlying masses the result of lymphatic permeation.

disease. It is not homogeneous but dotted here and there with pale yellow dots and streaks. These represent necrotic cells. On scraping the surface a milky fluid is obtained, to which the name of "cancer juice" has been given. The cut surface is slightly concave, retracting below the general level of the breast. Contrast this with chronic mastitis in which the surface does not change, and with fibroadenoma

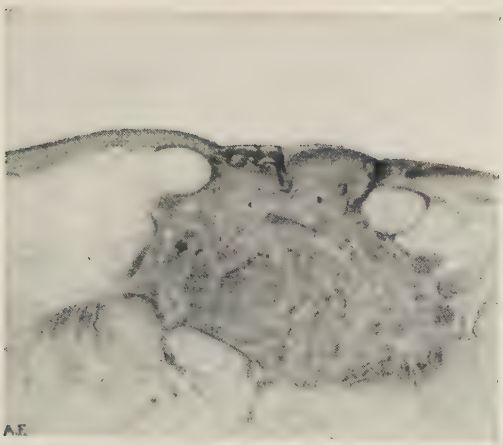

FIG. 221.—Carcinoma of the breast showing retraction of the nipple and limited invasion of the fat. (MacCallum.)

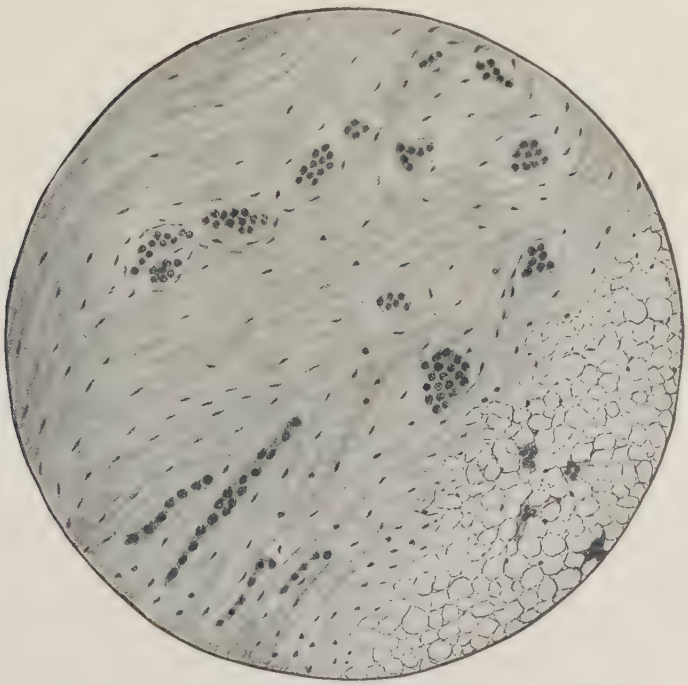

FIG. 222.—Scirrhous cancer of breast. The type of growth is carcinoma simplex, the cells being arranged in solid masses and columns.

which bulges forwards whenever it is exposed. Cysts may be present, but are not a characteristic feature.

We would emphasize here the great importance of the naked-eye inspection of breast tumors. Some surgeons, such as Halsted and Bloodgood, trust entirely to this method and do not have recourse to a rapid frozen section. When available the service of the microscopist should be accepted, but it ought to be generally realized that in the vast majority of cases the gross appearance of carcinoma of the breast

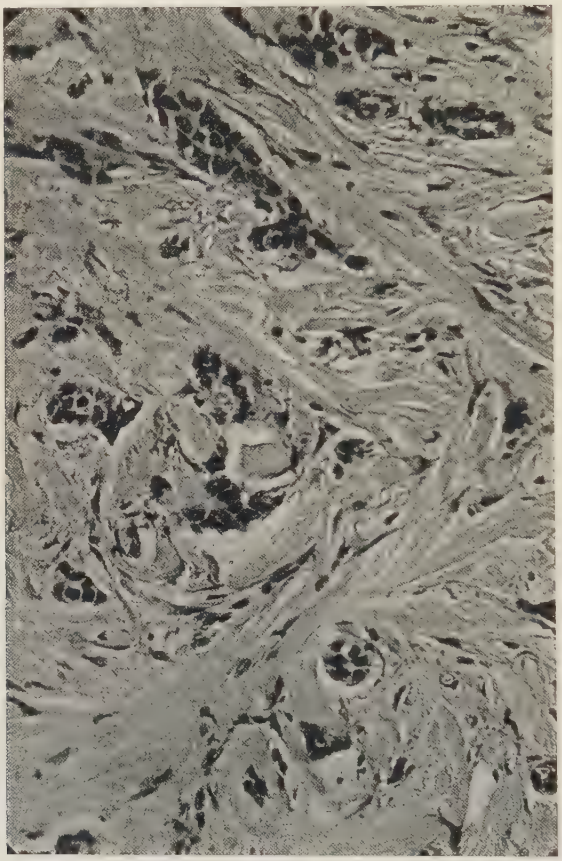

Fig. 223.—Scirrhous carcinoma of the breast. The masses of compressed cells with hyperchromatic nuclei are separated by an abundant and dense stroma. (Ewing.)

is as characteristic as the frozen section picture; in some cases it is more so, and less liable to lead to error. In every doubtful case the breast should be carefully explored at the beginning of the operation. If carcinoma is found the cut surface is treated with pure carbolic followed by alcohol, the wound closed, and the radical operation performed. The surgeon cannot always have a pathologist at his elbow to make rapid sections for him, but he can learn to recognize the

typical look of a breast carcinoma, and until he does so it would be better if he confined his activities to other fields.

Microscopic Appearance.—There is no trace of normal breast structure. The epithelial cells are collected in small masses or columns, but they may be actually in single file. Being compressed by the fibrous tissue they are usually polygonal or distorted, and may be small and dark staining. There is no attempt at glandular formation. Mitotic figures are rare. The stroma is dense and abundant, often scar-like in appearance. Indeed so dense may be the stroma that in any given section there may not be a single epithelial cell visible. In such a case a mistake in diagnosis is liable to occur unless more than one section be examined. It is denser at the center than at the periphery. Patches of round-celled infiltration are common. The unaffected part of the breast may show in places the changes characteristic of chronic mastitis.

Carcinoma, Fibroadenoma, and Chronic Mastitis Contrasted.—In each of these three conditions the patient complains of a lump in the breast. In chronic mastitis there is a finely granular induration, often confined to one wedge-like sector of the breast, which may be multiple, and which is only vaguely palpable to the palm of the hand. It is not adherent to the skin or deep fascia, the nipple is not retracted, and the axillary glands when enlarged are small and tender.

In fibroadenoma the mass is single or multiple, sharply circumscribed, not attached to the skin or deep fascia, and the axillary glands are not enlarged.

In carcinoma the lump is single, hard, not confined to one sector, neither painful nor tender, palpable to the palm of the hand; the nipple may be retracted, and the axillary glands considerably enlarged but not tender.

On section the mass in chronic mastitis is indefinite in outline, tough and indiarubbery in consistence, of a yellowish-grey color, and cysts of varying size are common. The fibroadenoma is circumscribed, encapsulated, and easily shelled out, firm, white in color, homogeneous or finely granular, and when incised it feels hard, but neither tough nor gritty. Carcinoma is irregular in shape, indefinite in outline, firmly adherent to the surrounding fat, densely hard, grey in color but not homogeneous looking, cuts with a peculiar gritty feel, and "cancer juice" may be scraped from the surface.

Carcinoma may arise in a breast already the seat of chronic mastitis, so that the two conditions frequently co-exist. It may also be associated with fibroadenoma, but does not arise from conversion of that tumor into a malignant growth.

The less common varieties of cancer of the breast may now be briefly considered.

Medullary or Encephaloid Carcinoma.—When the glandular proliferation is marked in comparison with that of the connective tissue, a soft, rapidly growing tumor results, which invades the skin, ulcerates, and appears on the surface as a large fungating mass. Unlike

a scirrhus the tumor is very friable so that little pieces can be picked out with a knife. The axillary glands enlarge rapidly, and the course of the disease is comparatively quick.

Microscopically, masses of large, rounded epithelial cells, much paler than those of a scirrhus, are separated by a scanty and relatively delicate stroma. Mitotic figures are numerous, and degenerations are common and extensive.

Adenocarcinoma.—Several forms of this somewhat uncommon breast tumor have been described, and it is difficult accurately to define its exact limits. It is a columnar-celled carcinoma, and arises from the wall of a duct. It is probable that *duct carcinoma* should be

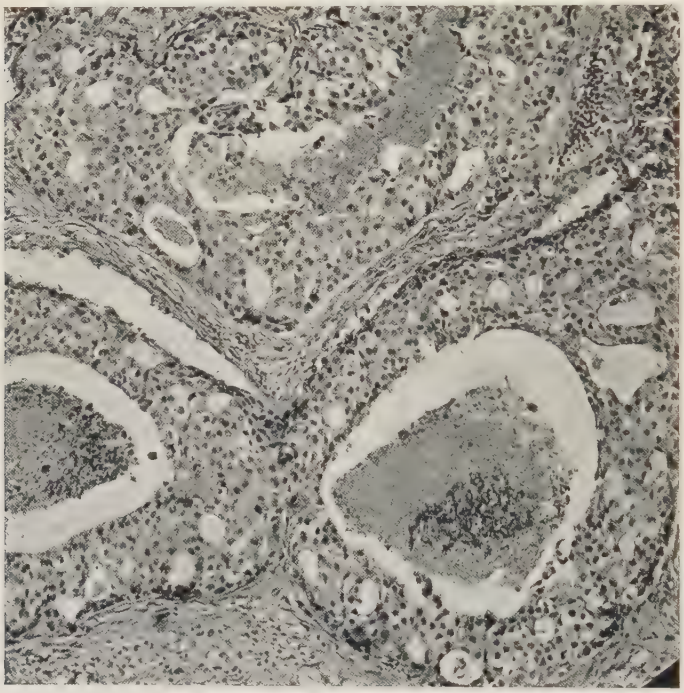

FIG. 224.—Mammary cancer. Adenocarcinoma of ducts, beginning to infiltrate. (Ewing.)

included in this class, although many authors describe the two conditions separately.

Gross Appearance.—The tumor presents a large number of small areas from which a worm-like cast can be expressed, so that Bloodgood has given the name comedo-carcinoma to this form of growth. These areas represent small cysts, which are dilated ducts filled with caseous carcinomatous masses. The tumor is much softer in consistence than the usual breast carcinoma. It is usually situated near the nipple, but never causes its retraction. The characteristic occurrence of a blood-stained discharge from the nipple has already been referred to

in connection with duct papilloma. The tumor is of slow growth and limited malignancy, and seldom gives rise to metastases in the lymphatic glands.

Microscopically the picture is that of irregular gland-like spaces lined by many layers of columnar cells, or there may be solid masses of cells lying within a tubular space. These cellular masses are often necrotic and easily dislodged. Papillary processes may project from the walls of the dilated duct into the lumen. It is by no means improbable that in many cases the glandular arrangement may be fictitious, being accounted for by the interlocking and fusion of a number of papillary processes. The same question has already been considered in the case of duct papilloma (page 545). It appears probable that in a number of cases a duct papilloma may develop into a duct carcinoma.

Acute Carcinoma.—In this form there is rapid dissemination of the growth throughout the breast and in the skin. It generally develops during lactation. As the breast is inflamed and swollen, and the skin hot and red, the condition may be mistaken for acute mastitis. The appearance of secondary nodules in the skin is diagnostic. Death results within three months.

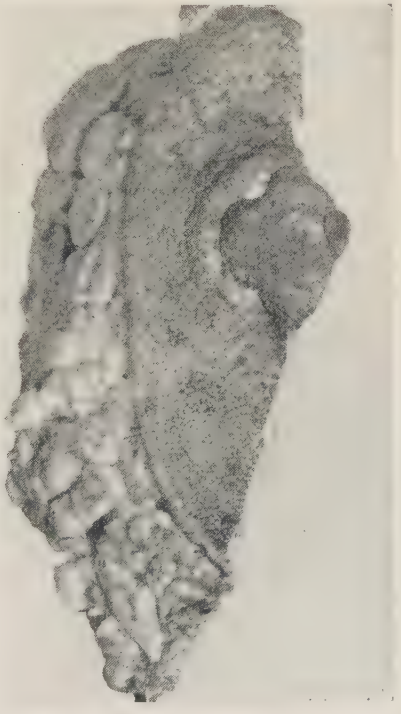

Fig. 225.—Paget's disease of the nipple.

PAGET'S DISEASE OF THE NIPPLE

This interesting condition, first described by Sir James Paget in 1874, is one which has aroused great discussion for many years, and a variety of views have been held as to its nature.

It commences as an intractable eczema of the nipple, but sooner or later, usually within two years but occasionally not for as long as ten, a carcinoma appears in the breast, frequently at some distance from the nipple. The eczematous area is usually bright red and inflamed-looking, with a finely granular surface. The surface may be moist and weeping, or dry and scaly.

The chief subject of debate has been whether the eczema precedes the tumor, or the tumor the eczema. Which is primary? There can be no doubt now that Paget's disease of the breast is essentially a malignant condition, and that the eczema is the result of the carcinoma. The recent work of Sampson Handley is particulary convincing.

According to Handley the disease begins as a carcinoma of atrophic type and slow growth. The tumor is often a duct papilloma, commencing in one of the smaller ducts, but not producing a palpable tumor for a considerable time. The lymphatic vessels become permeated, and presently the lymphatic block extends as far as the subareolar plexus beneath the nipple.

The lymphatics of the skin originate as blind finger-like processes in the papillæ of the dermis; these processes continue downwards and empty into a collecting vessel which joins the fascial plexus. Permeation or merely blockage of these vessels will soon result in edema of the nipple and surrounding skin, which will be accompanied

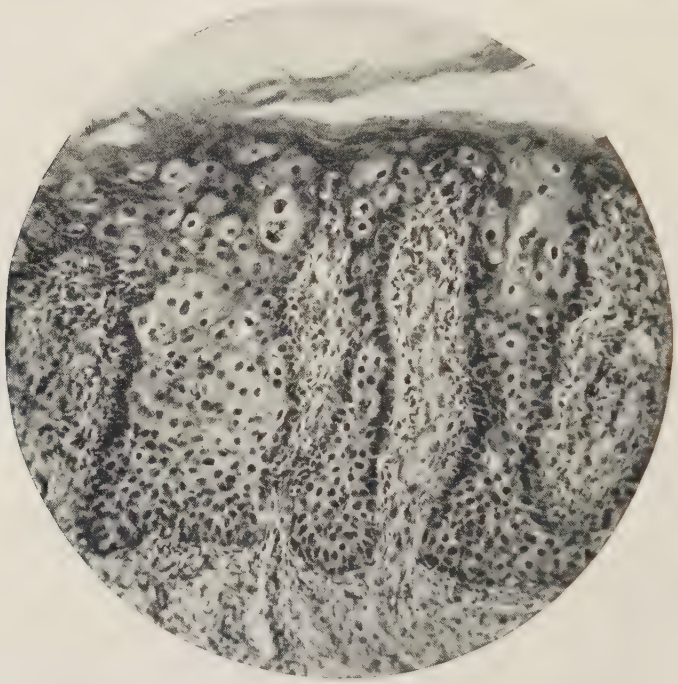

Fig. 226.—Paget's disease. Epidermal hyperplasia, edema, vacuolation, loss of prickles and multinuclear cells. (Ewing.)

by eczema and by some of the histological changes associated with Paget's disease. In one of my own cases, which Sampson Handley considered to be a particularly early example, the permeation of the subareolar plexus and the accompanying round celled infiltration were very clearly seen.

Microscopic Appearance.—There are three characteristic features to be looked for in a case of Paget's disease. These are (1) epidermal hypertrophy, (2) the presence of Paget cells, and (3) subepidermal round cell infiltration.

1. Epidermal hypertrophy, before ulceration has taken place, is a constant feature of the disease, and is probably due to the lymphatic

edema. The epidermis may be two or three times its normal thickness, and the epidermal papillæ are increased both in depth and in width.

2. Paget cells, so-called, are large, clear, vacuolated cells with small pyknotic nuclei. They look like clear spaces punched out of the epidermis. They appear first in the middle layers of the epidermis. At one time supposed to be infected with psorosperms, these hydropic cells are now recognized to be merely the result of the edema following the lymphatic obstruction.

3. The superficial part of the dermis shows the infiltration with round cells and plasma cells and the perilymphatic fibrosis which follows on the heels of lymphatic permeation. The ducts are dilated and filled with epithelial cells. Portions of actual carcinomatous tissue may or may not be present in the section.

Sarcoma.—Although by no means a common tumor, sarcoma of the breast is not so rare as used to be supposed. It may commence as a

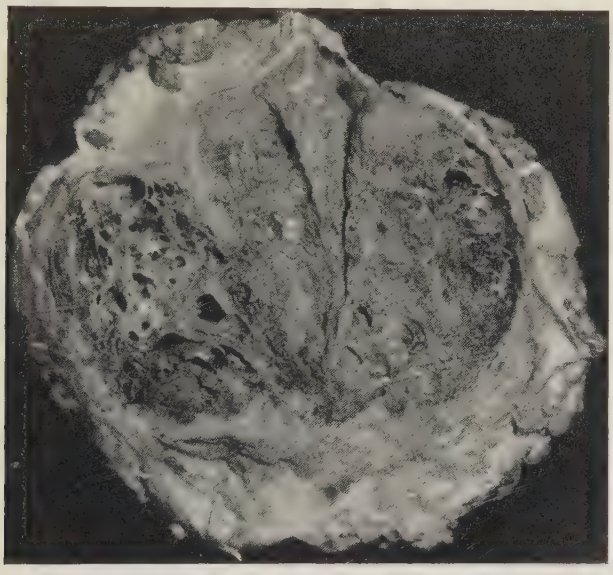

Fig. 227.—Angioma of the breast.

sarcoma, or may result from sarcomatous transformation of an intracanalicular fibroadenoma. It may be round-celled or spindle-celled in type. Occurring during the same age periods as carcinoma, it differs from that disease in its rapidity of growth, and in the fact that there is no coincident atrophy of the other tissues of the breast, which accordingly becomes greatly enlarged. The tumor ulcerates through the skin, and sets up secondary growths in the viscera and bones. The axillary glands are generally not enlarged.

Many other tumors such as lipoma, myxoma, chondroma, and chondrosarcoma may occur in the breast. They are very rare and do

not call for any special consideration. An angioma may cause serious hemorrhage if incised during an operation.

TRAUMATIC FAT NECROSIS

In 1920 Lee and Adair described a condition of the breast of great interest to surgeons and pathologists. Following an injury to the breast, usually hypodermoclysis, a tumor made its appearance which in the earlier cases was mistaken for carcinoma, but proved to be the result of an inflammatory reaction around an area of necrotic and liquefied fat. The pathological work was done by Ewing.

Clinical Features.—The incidence of the disease at the Memorial Hospital, New York, in comparison with primary breast carcinoma was 1.8 per cent. Of the five cases described in the original paper and in a subsequent article the youngest was 36, the oldest 54. In every instance the patient was corpulent (the lightest weighed 152 pounds, the heaviest 211 pounds), and the breasts were large and full, in one case reaching to the level of the umbilicus. All the cases gave a very clear and definite history of trauma to the breast. In three of the five cases there was a previous history of hypodermoclysis, in one a fall upon a spike. In only one case was there any complaint of pain. The mimicry of carcinoma was close, although the mass was fairly well circumscribed. A characteristic symptom was the extreme hardness of the tumor. The tumor was fixed to the skin in four cases, but to the deep structures in only two. The interval between the receipt of the trauma and the appearance of the tumor was very variable, from three weeks to ten years. The condition is essentially innocent, and only a very limited excision is necessary.

Gross Appearance.—The affected area is opaque, and may show one or more cysts containing liquefied fat; or the center may simply be somewhat diffluent. The area is more or less encapsulated; at least there is no evidence of infiltration. The cicatricial contraction and the yellow points and streaks of carcinoma are not observed. Although to a superficial examination there may be a resemblance between the gross appearance of carcinoma and traumatic fat necrosis, a careful study will reveal essential differences. It is possible to make a correct diagnosis on the operating table from the gross appearance.

Microscopic Examination.—Areas of necrosis and liquefaction in the fat are surrounded by abundant newly formed connective tissue, so that the picture is one of chronic productive inflammation in the fat. Giant cells of the foreign body type are numerous. The blood vessels show an obliterating endarteritis and a perivascular infiltration with lymphocytes. The general picture suggests syphilitic infection, but spirochetes were not found in the tissues.

CYSTS

Cyst formation is of common occurrence in the breast. It is customary to draw up elaborate classifications of cysts of the breast, but little is to be gained from this practice. The important cysts have

already been considered in discussing chronic mastitis. We have distinguished the single blue-domed cysts occurring in younger women, and the diffuse multiple small cysts seen in elderly women. Occasionally the breast is riddled with larger cysts—the classical cystic disease of the breast.

Very many of the cysts of the breast, particularly those known as involution cysts and the cysts of chronic mastitis, are regarded as retention cysts due to obstruction of the ducts from fibrosis. There is no proof of this theory; no one has ever demonstrated a duct being strangled by fibrous tissue. It is much more probable that the cyst formation is due to epithelial hyperplasia followed by involution.

The relation of cysts to such tumors as duct papillomas and intracanalicular fibroadenomas has already been dwelt upon.

FIG. 228.—Tuberculosis of breast. The condition was mistaken clinically for carcinoma.

A *galactocele* is a very rare condition in which a large cyst containing milk arises during lactation. It is situated close to the nipple, and pressure upon it causes milk to exude from the nipple. The cause of the obstruction is unknown.

Hydatid cysts are of such rare occurrence that they need only be mentioned.

TUBERCULOSIS

Tuberculosis is a rare disease of the human breast, although common in the udder of the cow. In the early stage a firm mass is pres-

ent, which may readily be mistaken for carcinoma. Later softening occurs, and tuberculous sinuses may be formed. The microscopic picture is characteristic.

SYPHILIS

A primary chancre with involvement of the axillary glands may occur on the nipple of a wet nurse infected by a syphilitic child. The chancre presents the usual features of a hard sore, and spirochetes can be obtained from the ulcerated surface.

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CHAPTER XXVIII

DISEASES OF THE ARTERIES AND VEINS

ACUTE ARTERITIS

For practical purposes acute inflammation of an artery, as of a vein, may be regarded as being bacterial in origin. It is true that the cut end of an artery becomes the seat of a plastic inflammation, but from the surgical standpoint the above statement may be generally accepted. This infection may reach the affected segment of vessel from without or from within. The first form commences as a periarteritis, the second form as an endarteritis.

1. *Acute Purulent Periarteritis.*—At first sight it appears somewhat remarkable that an artery, which traverses an abscess cavity and is constantly bathed in pus swarming with virulent organisms, does not in every instance develop an acute inflammation. As a matter of fact such an inflammation is by no means common, the reason being that the walls of the vessels are nourished by vasa vasorum which are separate from the main trunks, so that the vessel wall is able to offer very considerable resistance.

Not infrequently, however, this resistance is broken down, and the walls of the vessel become acutely inflamed and infiltrated with pus cells. The elastic lamina offers the stoutest resistance, but when it gives way severe and fatal hemorrhage may result. There may be a few small preliminary hemorrhages into a draining abscess before the final flood.

This accident is especially common in the neck in connection with peritonsillar abscesses which threaten the carotid artery. A tuberculous abscess of the lung may erode a branch of the pulmonary artery, and the cold abscess of Pott's disease may do the same for the vertebral artery.

Secondary hemorrhage, fortunately rare in these days of asepsis, is due to a periarteritis. The conditions for trouble are ideal. The vessel has been traumatized and separated from its surroundings, the inner and middle coats are lacerated, and a septic ligature is buried in the outer coat. The protecting thrombus which forms soon becomes infected and disintegrates, and it is then only a matter of time before the inflamed and weakened vessel gives way.

2. *Embolic Endarteritis.*—When an infected embolus lodges in an artery the result is a septic endarteritis. The source of the embolus is usually either an inflamed vein or an ulcerative endocarditis. The results have already been discussed in the previous section. Of these the most important are (1) a septic thrombosis, (2) the formation

of metastatic abscesses, and (3) the production, through local weakening of the vessel wall, of a small acute mycotic aneurism, which, giving way, may lead to severe and even fatal hemorrhage. Cerebral hemorrhage, as already remarked, may in this way complicate ulcerative endocarditis. If the artery blocked belongs to a terminal circulation the usual phenomena of infarction will result. The infarct, of course, will be a septic one.

3. *Subacute Non-pyogenic Arteritis.*—In addition to the two forms just considered, both associated with suppuration, there is another form of arteritis caused either by bacteria or their toxins, in which instead of a purulent infiltration involving all the coats there is an endothelial and subendothelial proliferation, although there may also be a mesarteritis. Such a condition, often associated with an undue tendency to thrombosis, may be found in typhoid, pneumonia, scarlet fever, septicemia, and other general infections.

The most interesting example of acute non-pyogenic arteritis is furnished by syphilis. This affects particularly the vessels of the brain and cord, where thrombosis is frequently associated, and the aorta. *Syphilitic aortitis* is a condition with very well defined clinical and pathological manifestations. It affects particularly the ascending portion and the arch of the aorta, owing probably, as Klotz has suggested, to the very abundant lymphatic supply of those parts. In the acute stage the lining of the aorta is quite red and inflamed-looking, and under the microscope the vasa vasorum in the middle and outer coats are surrounded by a collar of lymphocytes and plasma cells very similar to the perivascular collars seen in the brain in encephalitis lethargica. The spirochæta pallida, often in large numbers, can be demonstrated in the wall of the aorta.

In the late stages the gross appearance of the aorta is quite characteristic, and can readily be differentiated from atheroma, with which it used to be confused. The formation and contraction of scar tissue leads to a longitudinal wrinkling, some of the folds being pearly, others yellow and opaque. The ulceration and calcification so characteristic of atheroma are not found in syphilis owing to the greater vascularity of the newly-formed tissue. There is, however, great fragmentation and destruction of the elastic fibers, with consequent weakening of the vessel wall and a tendency to aneurism formation, a point which will be considered more in detail presently.

PHLEBITIS

Inflammation of a vein has many points in common with inflammation of an artery. Thrombosis, however, is much more frequently associated with the inflammation, so frequently, indeed, that the condition is often referred to thrombo-phlebitis. The thrombosis advances ahead of the inflammation. On this account hemorrhage is rare compared with the similar condition in arteries. The relation between phlebitis and thrombosis is a reciprocal one. The phlebitis

usually gives rise to the thrombosis, but a thrombus, acting as a mechanical irritant, may set up a phlebitis.

Many classifications of phlebitis have been suggested, from the plastic, suppurative, and ulcerative forms of John Hunter to the much more complicated recent classifications. Taking the broadest view we may consider phlebitis as being either (1) non-suppurative or (2) suppurative.

Non-suppurative Phlebitis.—When a vein is ligatured and thrombosis occurs, an aseptic phlebitis is set up, that is to say the phenomena ensue which are associated with repair. A plastic exudate is formed on the ruptured inner coat, new vessels grow into the thrombus from the vasa vasorum, and organization proceeds in an orderly manner. The results of thrombosis have already been discussed (page 142). When one of the main veins of a limb is occluded the part becomes white and develops a kind of solid edema, which may persist for years.

In chlorosis, gout, cachexia, and other constitutional disturbances what may be termed a toxic phlebitis associated with thrombosis may occur. The changes in the vein wall are degenerative and destructive rather than inflammatory, and appear to be due to the hypothetical toxins which are supposed to circulate in the blood in these conditions. Our knowledge of these, however, is so scanty that little can be said on the subject. Many cases of aseptic thrombosis following operation may be included in this group.

Much more important than either of the foregoing is a group in which phlebitis is due to the action upon the vessel wall of bacteria which are non-pyogenic or of relatively low virulence. Phlebitis associated with thrombosis is accordingly seen in such conditions as typhoid, pneumonia, scarlet fever, influenza, or may follow operations on inflammatory conditions such as appendicitis. The process may be a true inflammation, but does not go on to suppuration.

Suppurative Phlebitis.—From the view-point of the surgeon this is by far the most important variety of phlebitis. It is caused by pyogenic bacteria. The infection, in the great majority of cases, invades the vein from without, the phlebitis being preceded by a cellulitis of the surrounding tissue. This cellulitis may extend along the course of the vein, so that the phlebitis has every facility for extension.

The wall of the vein is infiltrated with leucocytes, just as in acute arteritis. Thrombosis rapidly occurs. The clot softens and mingles with the pus from the vessel wall. Hemorrhage is not common for reasons already discussed.

In other cases the inflammation may be due to pyogenic bacteria carried directly to the wall of the vein, with the early formation of a septic thrombus. Such a condition commences as an endophlebitis rather than a periphlebitis, and is accordingly much more in line with acute arteritis which is so frequently dependent upon the impaction of a septic embolus in the lumen of the vessel.

Suppurative phlebitis is seen in any part of the body following operations or secondary to purulent inflammation. The condition has every inducement to spread along the vein, a spread which may prove fatal unless the part is opened up and the inflamed and thrombosed vein tied off from the general circulation.

Some of the most notable examples of suppurative phlebitis are as follows: phlebitis of the lateral sinus following acute inflammation of the middle ear, and threatening to extend down the internal jugular vein; phlebitis of the facial veins following a boil or carbuncle of the upper lip, extending through the ophthalmic veins to the cavernous sinus; phlebitis of the hemorrhoidal veins following operations on the hemorrhoidal plexus or the rectum; phlebitis extending from the appendix to the portal vein; phlebitis of the mesenteric veins following suppurative conditions of the intestine and threatening gangrene of the bowel from the obstructive thrombosis; thrombosis of the pelvic veins following puerperal sepsis or operations on the uterus and appendages, spreading along the veins of the broad ligament to the external iliac and femeral veins; phlebitis of the veins of the leg in cases of varicose veins with ulceration and other septic conditions in that region.

ARTERIAL DEGENERATIONS

Here we enter upon a subject of great difficulty, confusion, and obscurity. Our ignorance regarding the nature and causation of these conditions is so great that it is but natural that we find ourselves threading our way amidst a maze of hypotheses with only here and there a well-established fact on which we can rely, looking in vain for some general principle on which to take a stand. We hardly know if we are dealing with one or many conditions, or if they should be considered primarily as degenerations or chronic inflammations.

The subject is usually regarded as belonging to the realm of the internist. It is, however, becoming of ever-increasing importance to the surgeon. Not only do the local effects, the lack of nutrition leading to gangrene of an extremity, and so forth, demand immediate consideration, but the influence of arterial disease on the patient in general, lowering his resistance to infections, trauma, and shock, rendering him more liable to post-operative intoxications, and interfering with his powers of reaction so that what in a young person with healthy vessels would be a short acute inflammation in a senile patient with arteries like pipe-stems becomes a long-drawn-out affair which may terminate in gangrene: all these make a claim on the surgeon's attention which cannot be ignored.

The matter of classification is one of great difficulty, as is always the case when our knowledge of a subject is fragmentary and incomplete. The following is less unsatisfactory than some which have been used.

1. Arteriosclerosis:
   a. Nodular—intima primarily affected.
   b. Medial—media primarily affected.
2. Endarteritis obliterans.
   a. Functional sclerosis.
   b. Thromboangiitis obliterans.
3. Syphilitic arteritis.

1. **Arteriosclerosis.**—This term is sometimes applied to all forms of arterial thickening. It is desirable, however, to confine it to a very definite form of degenerative change.

The typical *nodular* form of arteriosclerosis to which the name of *atheroma* is applied affects the large arteries such as the aorta and its direct branches, and the small arteries such as the coronary and cerebral arteries. The medium sized vessels such as the radial and the tibials are more liable to a *diffuse* degeneration associated with senile changes. The former is preeminently a disease of the intima, the latter a disease of the media.

Nodular Sclerosis or Atheroma.—The nodular variety may be studied in its classical form in the aorta. The disease is commonest in the arch of the aorta and around the openings of the intercostals, but it may affect the abdominal aorta to a marked degree, thus differing from syphilitic aortitis.

In the earliest stages slightly raised longitudinal streaks and patches appear, at first pearly and translucent, but soon becoming yellow and opaque owing to fatty degeneration in the deeper layers. As the disease advances the patches become more prominent and may coalesce, so that large areas are involved. These irregular elevated plaques have been likened to drops of paraffin. When the patch is incised it is found to contain a soft, mushy, pultaceous material somewhat resembling porridge. It is from this appearance that the disease derives its name of atheroma, from the Greek ἀθηρη meaning gruel. The term atheroma should be confined to this form of the disease and not applied indiscriminately to any form of arterial degeneration.

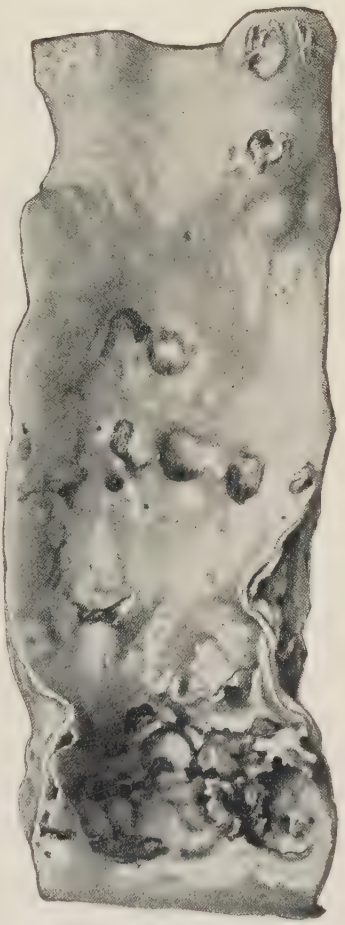

Fig. 229.—Late stage in atheroma of the aorta: ulceration and calcification. (MacCallum.)

Lime salts are deposited in the necrotic material, so that the vessel becomes studded with crackling calcareous plates. The mechanism of the calcification is as follows. The fat, which is present in the form of esters of glycerine and cholesterin, is saponified into glycerine and cholesterin on the one hand and fatty acids on the other. Calcium unites with the fatty acid to form an insoluble soap, which is deposited in the tissues, and in time phosphoric acid replaces the fatty acid to form hard calcium phosphate. The surface endothelium and the superficial fibrous layer may now give way, so that the atheromatous material becomes exposed and an *atheromatous ulcer* is formed

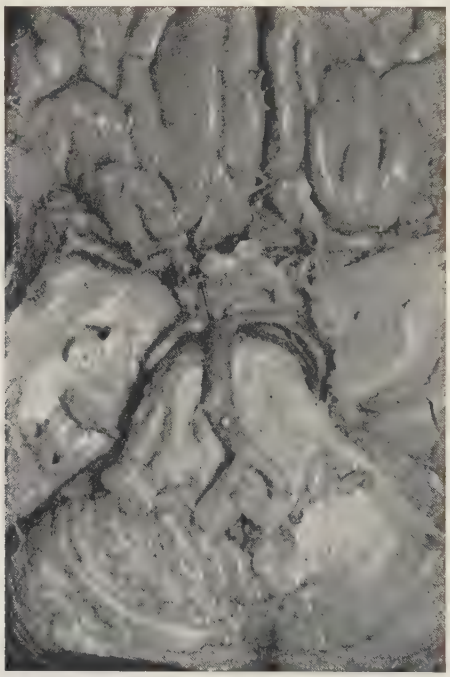

Fig. 230.—Atheroma of cerebral arteries. Small atheromatous patches are scattered along the basilar artery and the vessels of the circle of Willis.

on which platelets and fibrin are very readily deposited with the production of a thrombus.

Microscopically the change is seen to be essentially one of the intima, although the media may be secondarily involved. In the early stages the patch consists of a mass of new-formed cellular connective tissue in the intima. Even at this early stage fatty degeneration is pronounced, the cells containing the fat droplets being found in the superficial as well as the deeper parts of the patch. In the later stages there is an amorphous mass in the depths of the intima made up of droplets of neutral fat, doubly refractive cholesterin esters, cholesterin

crystals represented by needle-shaped spaces in the tissue, and granules of calcium and magnesium phosphates staining blue with hematoxylin.

This atheromatous mass is covered by a hillock of dense connective tissue, containing hardly any cells, almost entirely avascular, but not as a rule much degenerated.

FIG. 231.—Medial sclerosis of Mönckeberg in a femoral artery in longitudinal section. The calcified rings are seen in cross-section. (MacCallum.)

The internal elastic lamina becomes fragmented or broken into laminæ, a most important change, as it interferes seriously with the elasticity of the vessel, and therefore predisposes to irregular dilatation and aneurism formation.

The media under the plaque, apart from some thinning, cellular infiltration, and slight fatty degeneration often shows comparatively little change. It must be mentioned, however, that some authorities consider that the primary lesion consists of a weakening of the media, and that the thickening of the intima is merely compensatory.

Sites.—Atheroma occurs in the aorta, both thoracic and abdominal, and in the large main branches which arise from it, such as the carotid, the renal, the splenic, etc. The pulmonary artery may be involved in mitral stenosis. The small arteries, especially the coronaries and the cerebral vessels, are very frequently affected. In these vessels the

Fig. 232.—Atheromatous arteries in a man of sixty-one shown by the X-rays. (Keen's Surgery.)

atheromatous plaque may lead to great narrowing of the lumen with the production of thrombosis. Moreover the weakening of the wall, which is an inevitable consequence of such serious degenerative changes, is the most important cause of cerebral hemorrhage. The cerebral vessels which are most affected are those forming the circle of Willis and the small branches of the middle cerebral to the basal ganglia, particularly the lenticulo-striate which has been called "the artery of cerebral hemorrhage."

Medial Sclerosis.—The medium sized arteries such as the radial and tibials and even vessels of larger size such as the femoral and the popliteal, although not often attacked by true atheroma, are very frequently the site in later life of a peculiar degeneration of the media known as Mönckeberg's sclerosis. The vessels of the lower limbs are the chief sufferers. The intima is comparatively little affected, but in the media there are extensive degenerative changes, at first fatty in character, but soon followed by a profound degree of calcification. Large patches of calcareous matter fuse and often encircle the vessel, giving it a ringed appearance like the trachea. The pure lesion does not give rise to any narrowing of the lumen of the vessel.

The thickening of the superficial arteries of medium size, so characteristic of old age, the pipe-stem radials, the prominent and tortuous temporals, are examples of Mönckeberg's sclerosis. If the aorta is affected it becomes sinuous and curves from side to side of the vertebral column.

Although Mönckeberg regarded the condition as being entirely different from atheroma, the two forms of degeneration are not infrequently combined, and there may be a great proliferation of intima internal to the calcified rings, leading to so extreme a degree of narrowing that only a pin-point opening is left. Such stenosis is usually very limited in extent, but several such narrow places may be found in the course of a single artery. The nutrition of the part, usually the leg or foot, will be seriously interfered with, and this is the usual cause of senile and diabetic gangrene.

Etiology.—The cause or causes of arteriosclerosis are at present unknown. Many have been suggested, but with none are we on sure and certain ground. Alcohol, syphilis, gout, lead, chronic Bright's disease, high blood pressure, and a score of others have at different times been the favorite of the day.

The relationship of high blood pressure to arteriosclerosis is confidently asserted, but should be accepted with reserve. The fact that the two are frequently associated is no proof of causal connection, for they both occur at the same age periods. In many cases of advanced arteriosclerosis the blood pressure is normal. The fact that arteriosclerosis of the pulmonary artery is sometimes found in cases of mitral stenosis does not carry conviction, for in many cases there is no such association, and Leonard Rogers has shown that in India it frequently occurs apart from any lesion of the mitral valve.

Repeated injections of adrenalin produce degeneration with calcification of the media. Russian workers such as Chalatow and Anitschkoff have been able recently to produce degeneration and thickening in the inner coat of the aorta by feeding rabbits with cholesterin. These results, although interesting, do not bring us much nearer the solution of the problem.

It would appear that arteriosclerosis is a vascular degeneration which may be brought about by a number of causes, just as fatty degeneration may be produced by a variety of agents. Of these the

two most potent are probably old age associated with the general wear and tear of life, and the action of toxins, bacterial or otherwise.

Arteriosclerosis is an almost inevitable accompaniment of old age. Clifford Allbutt expresses this in his own inimitable way: "Marvellous as in the human frame are the symmetry of parts and the harmony of function, yet it cannot be supposed that the stealthy hours carry away no qualities of tissue, no quantities of energy." But old age is a relative term. "A man is only as old as his arteries," and much depends upon the kind of arteries with which he starts out. Sometimes all the members of a family may show a tendency to early arteriosclerosis, a tendency which, as Osler remarks, can only be explained by supposing that in the make-up of the machine bad material was used for the tubing. Bad tubing put to a good use may be expected to break down, but only too often good tubing put to a bad use leads to a similar result.

Apart from old age, the most probable cause of arterial degeneration is the action of circulating toxins on the intima. What these toxins are we do not yet know, and it is better to acknowledge our ignorance than to suggest a list of hypothetical and unproven causes.

In this discussion we have carefully differentiated between arteriosclerosis, a true degeneration, and those more or less frankly inflammatory conditions such as syphilitic arteritis and endarteritis obliterans about to be described.

2. **Endarteritis Obliterans.**—The two varieties of arterial degeneration just described, the nodular and the medial, are well defined. We now come to a more heterogeneous group in which the distinguishing feature is a uniform proliferation of the inner coat leading to great narrowing of the vessel. One of the best recognized varieties, syphilitic endarteritis, will be considered separately.

Heterogeneous though the group may be we can distinguish two main types of cases.

1. Those in which narrowing of the lumen occurs in response to a lessened physiological demand.

2. Those in which a true inflammatory element appears to be present. The former may be called functional sclerosis, the latter thromboangiitis obliterans.

Functional Sclerosis.—The arteries of organs such as the uterus, ovaries, and breast, which are subject to marked periodic fluctuations of functional activity, often show great thickening of the inner coat with narrowing of the lumen during the involutionary period of life. During the height of functional activity the vessels are greatly dilated, but now that blood is no longer required in large amount there is a corresponding narrowing. The alteration is more than a mere hyperplasia of the inner coat. An entirely new vessel consisting of intima, media, and adventitia is formed within the lumen of the old one, owing apparently to a wandering inward of cells from the old coats. At the same time there is considerable thickening of the inner coat.

The obliteration of the temporary vessels in granulation tissue is effected by a similar mechanism. Beautiful examples of endarteritis obliterans are seen in the neighborhood of healing wounds. The intimal thickening so characteristic of the granular contracted kidney may have a similar explanation.

Thrombo-angiitis Obliterans.—Most forms of arterial degeneration occur after middle age, although it must not be forgotten that a man is only "as old as his arteries." There is, however, one peculiar and well-defined condition which occurs in comparatively young men between the ages of twenty and forty, and which is largely although not entirely confined to Russian and Polish Jews. As the veins as well as the arteries are affected throd anmbosis is constantly present the condition is known as thrombo-angiitis obliterans. A remarkable feature of the disease is that only the vessels of the lower extremity are involved.

The studies of Buerger have made it evident that the condition is inflammatory in nature, and that the occlusion and thrombosis are not due to a merely degenerative thickening of the inner coat. In that part of the vessel in which thrombosis has occurred the media and the adventitia are infiltrated by inflammatory cells, sometimes to a very marked degree. The inflammatory changes never extend into the wall of the vacant portions of the vessel. The intima usually shows a moderate amount of thickening, but this is never sufficient to account for the occlusion of the lumen and the thrombosis. Indeed in one of the few cases which I have had the opportunity of studying there was practically no thickening of this coat.

The lumen is occluded by a thrombus which must be ascribed to the presence of the inflammation in the vessel wall. The thrombus becomes organized and blended with the inner coat, so that the lumen is filled with a mass of vascular granulation tissue which may become canalized by endothelium-lined spaces through which a little blood may filter. There is none of the calcification so characteristic of Mönckeberg's sclerosis, so that in an X-ray picture the vessels cast no shadow, nor is there the fraying out and destruction of the internal elastic lamina so often seen in atheroma.

The cause of the disease is unknown, but Rabinowitz has recently succeeded in isolating a Gram-negative motile bacillus both from the blood of the local affected portion and from the blood stream. When this organism was injected into the ear of a rabbit it produced gangrene not only in the ear but also in the feet of the rabbit, and the vessels of the foot showed the same changes as are found in the human lesions.

The clinical phenomena are quite characteristic. The patient, a young Russian Jew, suddenly feels pain, burning, and tingling in the legs and feet, and observes that these parts are pale and cold. No pulse can be felt at the ankle. He is only able to walk a short distance before violent cramp-like pains develop in the legs, owing to the insufficient blood supply to the muscles, a condition known as intermittent claudication, and not infrequently seen in horses. Finally

gangrene of the toes may develop, spreading up so as to involve the foot and leg, and often necessitating amputation at the thigh.

This form of arterial disease can certainly be regarded as inflammatory in nature in comparison with the more purely degenerative arteriosclerosis. There are a number of other examples of endarteritis obliterans, apart from the functional variety already considered, all of which can probably be regarded as infective in nature. Syphilis produces a classical picture of endarteritis obliterans, undoubtedly due to

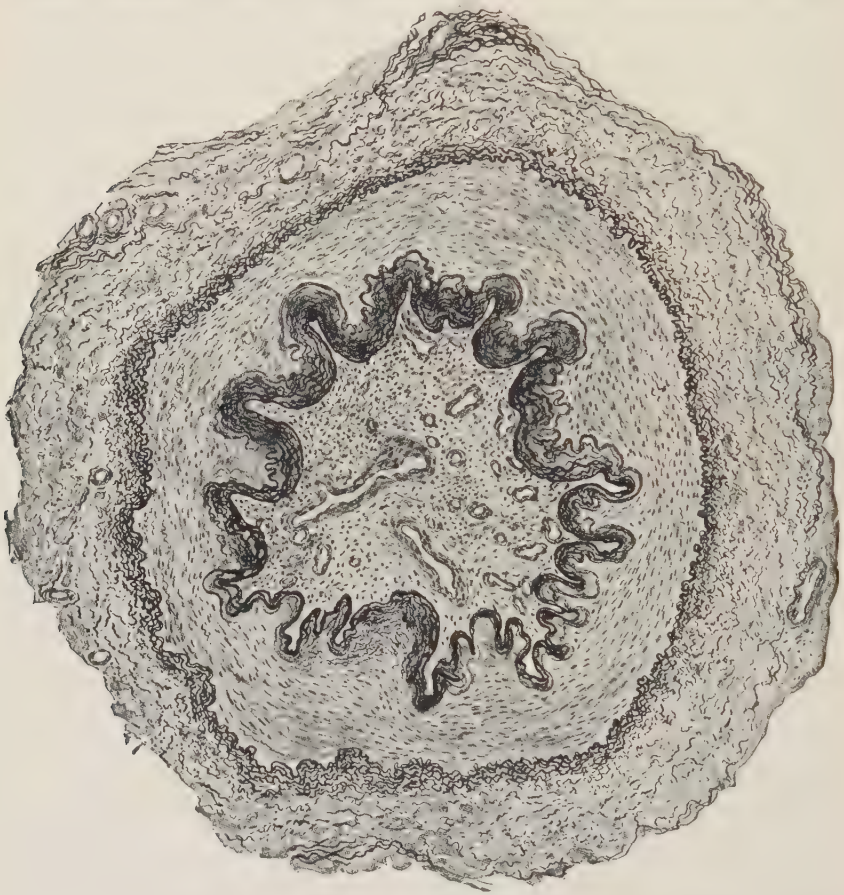

Fig. 233.—Thrombo-angiitis obliterans. Great thickening of the inner coat with partial recanalization. (MacCallum.)

the presence of the spirochæta pallida in the wall of the vessel. The arteries of any tissue the site of long-continued irritation will show a uniform thickening of the inner coat. One of the best examples is seen in the neighborhood of a tuberculous cavity. Another is provided by a gastric ulcer. In all of these cases it is the smaller arteries and arterioles which manifest the characteristic change.

3. **Syphilitic Arteritis.**—Syphilis of the blood vessels is now such a well-defined entity, and it has until recently been so frequently confused with atheroma and other forms of arterial degeneration, that it merits separate consideration.

Syphilis is primarily a disease of the blood vessels, the spirochetes reaching the vessels in the perivascular lymph spaces. Even in the primary sore the characteristic lesion is the perivascular round-celled infiltration and the thickening of the inner coat. The disease particularly affects, (1) the small arteries, and (2) the aorta.

FIG. 234.—Syphilitic aortitis; perivascular infiltration in the media, thickening of the intima.

Syphilitic Endarteritis and Periarteritis.—The changes may be studied in the small vessels in a syphilitic lesion, whether primary, secondary, or tertiary. They are seen in characteristic form in the meningeal vessels in a syphilitic meningitis.

The smallest vessels are surrounded by a collar of inflammatory cells, mostly lymphocytes and plasma cells. In somewhat larger arteries these cells may form collections in the adventitia which are practically small gummata, and which may undergo necrosis. The inner coat shows a regular thickening due to the formation of a young,

Table to show main characteristics of arterial degeneration.

	Disease	Artery affected	Coat chiefly affected	Probable nature of process	Age incidence	Ulceration	Calcification
Arterio-sclerosis	Nodular sclerosis	Aorta and small arteries.	Intima.	Degeneration.	Middle life or later.	Variable.	Variable.
	Medial sclerosis	Medium-sized arteries.	Media.	Degeneration.	Old age.	None.	Extreme.
Endarteritis obliterans	Functional sclerosis	Arteries of uterus and ovaries.	Intima.	Repair.	Involution period.	None.	None.
	Thrombo-angiitis obliterans	Arteries of leg.	Intima.	Inflammation.	Between 20 and 40.	None.	None.
	Syphilitic arteritis	Aorta and small arteries.	Media of aorta; intima of small arteries.	Inflammation due to spirochetæ.	Youth and middle age.	None.	None.

cellular, and vascular connective tissue, a condition of endarteritis obliterans. The vascularity of this new tissue, due to penetration of young vessels from the media and adventitia, prevents the degenerative changes which are so characteristic of arteriosclerosis.

Syphilitic Aortitis.—Syphilis of the aorta is of great frequency, and presents such a characteristic pathological picture that it is of special interest. Moreover it is the commonest cause of aneurism of the aorta. All three coats are affected, but the most serious changes are those in the media. Here again, however, it is the small vessels, the vasa vasorum, which are primarily involved.

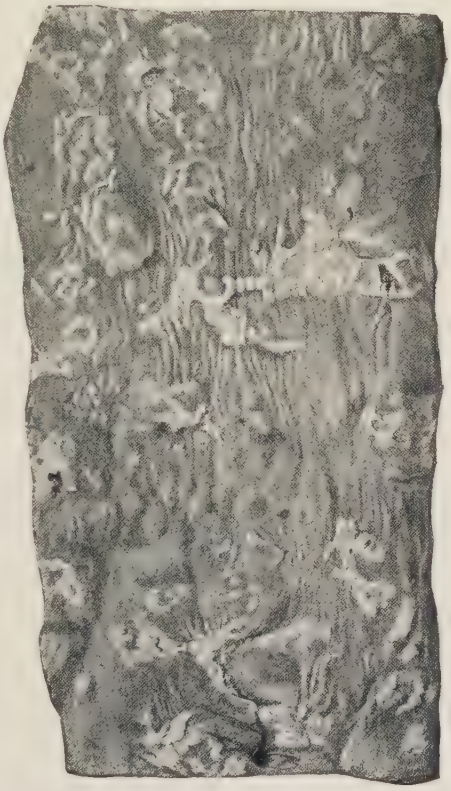

Fig. 235.—Gross appearance of syphilitic aortitis. The longitudinal wrinkling is well shown. (MacCallum.)

Microscopically the small cellular foci in the adventitia and in the media form a striking feature, by which the condition can be recognized at a glance. Sometimes they are rounded, but they are often in the form of linear streaks. Spirochetes in large numbers can be demonstrated by the Levaditi method, or better, by Warthin's modification of that method. The gummatous formation in the media plays havoc with the muscular and elastic tissue, and only the tattered remnants of elastic fibers may be found here and there. Necrosis is followed by fibrosis, and the subsequent scarring is responsible for the puckering which forms so characteristic a feature of the naked-eye picture. The new fibrous tissue is but a poor substitute for the elastic tissue, and the distension which follows each blood wave from the heart is no longer counteracted by the elastic recoil, so that there is an ever-present tendency to a progressive dilatation. The intima covering the affected patches of media undergoes a uniform fibrous thickening, probably compensatory in nature. There is a notable absence of the three features so characteristic of atheroma—fatty degeneration, calcification, and ulceration.

The *gross appearance* of the aorta is equally distinctive. The change begins at the commencement of the aorta, sooner or later involving the valves and producing aortic incompetence, extends upwards to the arch and the descending thoracic aorta, but stops

abruptly when it reaches the abdominal aorta, thus differing markedly from arteriosclerosis. The distribution is probably dependent upon that of the lymphatics. The interior of the aorta is puckered, ridged, and thrown into longitudinal folds. In the acute stage it is of a pinkish color, due to the intensity of the inflammatory changes. The intima over the affected areas is glistening and pearly. There are no calcareous plaques nor ulceration. The wall is much thinner in some places than others, and it is at these spots that an aneurismal dilatation is apt to occur. The whole aorta is usually dilated, and the dilatation may be uniform or saccular.

The *symptoms* of syphilitic aortitis are fairly constant. In the acute stages the most characteristic symptom is pain behind the sternum, often very severe. Palpitation and dyspnea are present. The X-ray shows a dilated aorta. The Wassermann test is positive.

ANEURISM

An aneurism is a localized dilatation of an artery. Almost any artery may be the seat of an aneurism, but the most important are the thoracic aorta and its main branches, the popliteal artery, and the cerebral arteries—both those entering into the circle of Willis and those passing to the basal ganglia.

Causes.—The essential cause is weakening of the arterial wall, especially when associated with a heightened blood pressure. The cause of the weakening may be (1) in the lumen of the vessel, (2) in the wall of the vessel, and (3) outside the vessel.

Of these far and away the most important is the second. As regards the first, an embolus, particularly if it be infected, will set up an inflammation in the arterial wall, which, through weakening the wall, may give rise to a mycotic aneurism, a complication of ulcerative endocarditis not infrequently seen in the cerebral vessels. Occasionally, though much more rarely, a simple aseptic embolus may, by the irritation it produces, act in the same way. Examples of the third type of cause are afforded by suppuration in the neighborhood of an artery or still better by the weakening produced by tuberculosis in the wall of an unsupported artery which traverses a tuberculous cavity. Serious pulmonary hemorrhage is often due to the rupture of such an aneurism, which is usually only miliary in size.

Disease or injury to the vessel wall itself, however, is the cause of those aneurisms which more particularly interest the surgeon. The principal cause of aneurism of the aorta is syphilis, which we have already seen to produce such great destruction in the middle coat. Atheroma also plays an important role in the aorta, and more particularly in the other large arteries such as the carotid and the innominate. It is probably the only cause of the dissecting form of aneurism.

A stab or bullet wound may give rise to a false aneurism, the walls of which are formed by the surrounding tissues instead of by the vessel wall.

Varieties.—A great variety of aneurisms have been quite unnecessarily described. We may, however, recognize a true and false aneu-

rism, a fusiform and sacculated aneurism, a dissecting aneurism, a cirsoid aneurism, a traumatic aneurism, and an arterio-venous aneurism.

A *true* aneurism is one in which the sac is formed by the coats of the vessel. When we say coats we really mean the outer coat. The middle coat of a true aneurism is always deficient.

A *false* aneurism is one in which the wall of the sac is constituted by the surrounding tissues. Such an aneurism is often traumatic in origin, and should rather be called a hematoma than an aneurism.

FIG. 236.—Dissecting aneurism of aorta. The middle coat of the aorta is occupied by a dark clot of blood.

A *fusiform* aneurism is a more or less uniform dilatation of the entire lumen of the vessel throughout an appreciable part of its length. It is found in the aorta, and occasionally in some of its large branches.

A *saccular* aneurism consists of a pouching of the vessel at one point. It may communicate with the main lumen by a narrow or a wide opening. It is the usual form of aneurism, and is commonest in the thoracic aorta.

A *dissecting* aneurism is one in which the blood has made its way through a ruptured atheromatous plaque into the middle coat, and has then proceeded up or down the vessel splitting the middle coat in its passage. Eventually it may open again into the lumen of the vessel, or it may burst externally. It is obvious that this is not a real aneurism, but rather a hematoma of the arterial wall.

Fig. 237.—Arterio-venous aneurism. The result of a gun-shot wound injuring the external iliac artery and vein.

A *cirsoid* aneurism is a peculiar and somewhat rare condition in which there is a mass of dilated and anastomosing vessels, each of which may possess numerous pouches. The corresponding veins are also involved. The condition, which usually develops fairly early in life, is progressive, and may recur when the vessels have been excised. From these characteristics it is evident that the condition is much more closely allied to a neoplasm than to an aneurism. The commonest site is the scalp. I saw a case in Edinburgh when house physician to Byrom Bramwell in which the entire scalp resembled a bag of worms.

A *traumatic* aneurism, again, is no real aneurism, but rather a hematoma. It is due to laceration of the arterial wall whereby blood is poured into the tissues, and by its pressure and irritation causes them to become matted together and to form a sac which limits its spread. The laceration may be due to a stab with a sharp instrument or the passage of a fragment of shell, leaving a very minute external wound. In other cases there is no such wound, for the rupture may be due to a sharp fragment of a fractured bone.

An *arterio-venous* aneurism is a condition which used to be a rarity, but which, as the result of the war, has become only too common. An abnormal communication between an artery and a vein is established. The cause is similar to that of a traumatic aneurism, namely the simultaneous wounding of an adjacent artery and vein by a bullet, piece of shrapnel, or pointed instrument. Occasionally the artery alone may be injured, the vein becoming secondarily involved a few days later. Even more rarely an ordinary non-traumatic aneurism may rupture into a vein. The common sites are those places in which a large artery and vein lie side by side, such as the neck, axilla, arm, groin, and thigh.

Two main varieties may be distinguished. In the first, the *aneurismal varix*, the blood flows directly from the artery into the vein. The veins below the communication become very tortuous and dilated, but the condition is usually not progressive. In the second, the *varicose aneurism*, there is an aneurismal sac between the two vessels into which the blood first flows. It tends to increase in size like any ordinary aneurism.

In both cases the distended veins pulsate almost as forcibly as arteries. A marked thrill can be felt and a loud hum heard over the aneurism. In one case to which I listened with a stethoscope the noise was terrific, reminding one of the interior of an engine shop. As the aneurism was in the neck the patient's chief complaint was the continuous noise in his head.

FIG. 238.—Aneurism of the heart which ruptured into the pericardium.

An *aneurism of the heart* may result from weakening of the wall of the left ventricle. The muscle is the seat of a fibrosis due either to syphilis or to loss of the blood supply from coronary artery disease and the weakened muscle is no longer able to withstand the strain of the intracardiac pressure.

Having briefly reviewed the various forms of aneurisms and pseudo-aneurisms, let us now consider somewhat more in detail a true saccular aneurism of such a vessel as the aorta.

The dilatation commences as a rule at the *arch of the aorta* in a vessel whose wall has been weakened by syphilis or arteriosclerosis.

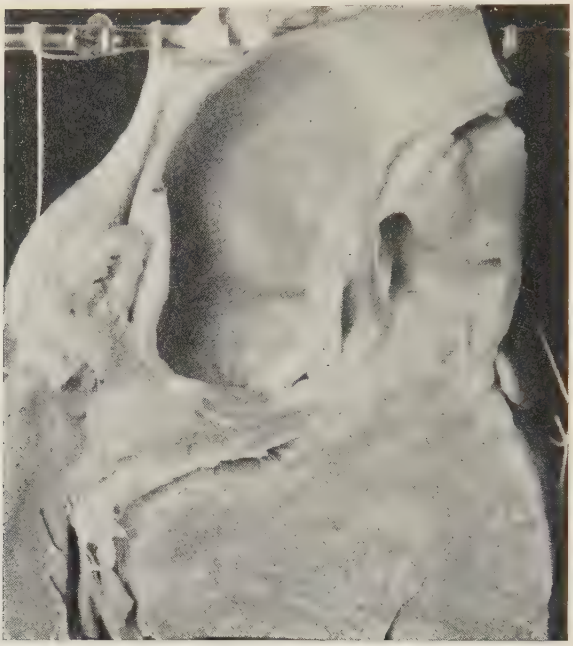

FIG. 239.—Aneurism of commencement of aorta, showing hypertrophy of wall of left ventricle.

FIG. 240.—Cavity in the lung produced by an aneurism of the aorta.

The mouth of the sac, often surrounded by atheromatous plaques, presents a rolled edge like that of an epitheliomatous ulcer. The sac may be of almost any size, and will press upon the adjacent structures. Thus it may grow forward and erode the sternum or ribs with great pain in the chest, or backwards and erode the bodies of the vertebræ, sparing the resistant intervertebral discs, and causing great pain in the back. It may press on the trachea with difficulty in breathing, on the esophagus with difficulty in swallowing, on the left recurrent laryngeal nerve with hoarseness and aphonia. It may rupture on the surface, or into the trachea, the bronchi, the esophagus, the pericardium, or the pleural cavity.

The lining of the sac is roughened owing to the endothelium giving way. Thrombosis occurs, and layer upon layer of laminated clot is

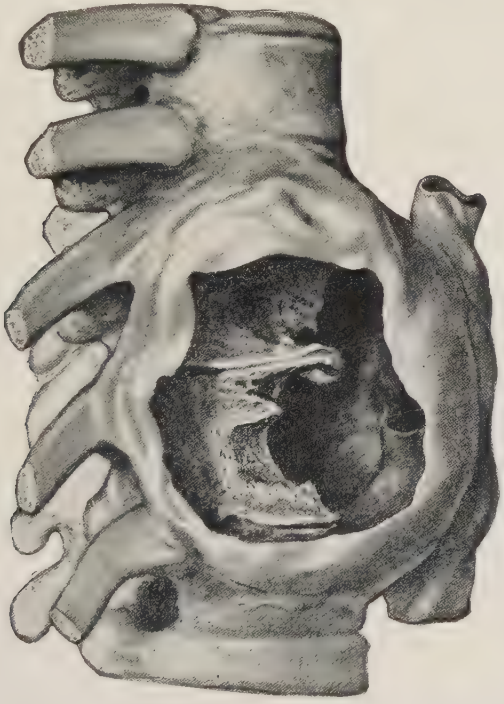

Fig. 241.—Destruction of vertebræ by aneurism. Dried specimen with aneurismal sac *in situ*. (MacCallum.)

rammed down and becomes incorporated with the wall of the sac. This is an attempt at spontaneous cure, and in the case of small aneurisms it is occasionally successful. The various operative measures employed are attempts to assist this natural process.

The **microscopic appearance** of the wall of the sac throws much light upon the nature of the condition. The middle coat of the aorta, composed of musculo-elastic tissue, is seen to end abruptly at the edge of the sac, and to take no part in the formation of its wall. The intima

is extremely flattened, and here and there the endothelial lining may be shed off. In the later stages it becomes indistinguishably fused with the laminated clot, but there is no evidence of any attempt to organize the clot. The connective tissue of the adventitia is incorporated with the compressed surrounding structures.

It is evident, therefore, that although a true aneurism is defined as one in which the wall of the artery enters into the formation of the sac, there is really not much of the original wall left.

For further information regarding aneurisms the reader is referred to the very exhaustive account by Matas in Keen's surgery, in which an extremely full bibliography is given.

VARICOSE VEINS

A varix or varicose vein is one which is permanently dilated, lengthened, and tortuous. Two chief types may be recognized. In the first, one main superficial vein with its tributaries is affected. In the second, a tangle of distended vessels occurs here and there in the course of a vein.

Sites.—Any vein in the body may become varicose, but there are only three common sites. These are: (1) the veins of the leg and thigh, particularly the internal saphenous; (2) the veins of the rectum and anus, the condition known as hemorrhoids; and (3) the pampiniform plexus of the spermatic cord, usually on the left side, the condition of varicocele.

Causes.—The *predisposing* cause, probably in a majority of cases, is a congenital weakness of the walls and valves of the veins. Several members of a family in successive generations may suffer from varix affecting the same vein and even the same segment of vein.

The *exciting* cause is anything which will bring about increased pressure in the vein. The following factors are important. (1) Central obstruction to the venous return owing to mitral disease, emphysema, or cirrhosis of the liver. (2) The pressure of a tumor, gravid uterus, or chronically loaded rectum. The pressure of tight garters is probably of little importance, although it may aggravate the condition once it is established. (3) Prolonged standing, whereby a long column of blood presses continually upon a weakened valve. (4) Straining and violent muscular efforts. The former aggravates the condition of hemorrhoids, the latter is responsible for the frequency of varicose veins in the legs of athletes.

Morbid Anatomy.—The essential lesion is a giving way of the valves, as a result of which all the other troubles follow. The vein becomes dilated and also lengthened; as a result of the latter tortuosity is inevitable. As a rule the disease is confined to one or more segments, but the vein may be involved in its entire length.

A phlebosclerosis develops, similar in many ways to arteriosclerosis. At first there is a hypertrophy of the musculo-elastic tissue in the media in response to the increased strain, but later atrophy occurs and

replacement by fibrous tissue. The intima also becomes fibrosed and thickened, and in places may greatly narrow the lumen of the vessel. The adventitia is similarly thickened, and the fibrosis may spread to the perivascular sheath, causing the vein to become adherent to surrounding structures. The walls of the vein may become quite brittle. The thickening is often irregular, so that here and there clusters of pouches may project through the thinner parts of the wall. In such pouches thrombosis will readily occur.

FIG. 242.—Varicose veins of the leg.

Effects.—The penalty for varicosity has to be paid partly by the veins, partly by the tissues which they drain.

The *veins* may rupture, either externally or into the tissues. The frequency with which this accident occurs in hemorrhoids has earned that condition its name. The bleeding from a varicose vein in the leg may be very profuse and long continued, owing partly to the incompetence of the valves, partly to the sclerosed condition of the vein which interferes with the natural arrest of hemorrhage.

Phlebitis is one of the most important complications. It is liable to occur owing to the stagnant condition of the blood especially in the pouches, to the diseased condition of the intima, and to the exposure of the superficial and dilated vessels to injury and infection. Lymphangitis is a frequent accompaniment of the phlebitis, and is responsible for much of the edema.

The *tissues* are chronically congested, and become infiltrated with serum. The skin becomes so sodden that a condition of chronic eczema develops, and the devitalized epithelium is liable to be abraded and ulcerated as the result of a trifling injury. The characteristics of a varicose ulcer, which is usually situated on the lower third of the leg, have already been described on page 63. Hemorrhage from a vein in the floor of the ulcer is of frequent occurrence.

The pressure of the dilated vein causes atrophy of the surrounding tissues. The structure to suffer most is the skin, and this thinning of the skin is another factor favoring ulceration. The skin of the lower part of the leg acquires a mahogany-brown or it may be a bluish tint. This is due to the deposit of pigment consequent upon the escape and disintegration of red blood cells.

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CHAPTER XXIX

THE SPLEEN

In order to understand the surgical pathology of the spleen, it is necessary briefly to consider the part which the spleen plays in the animal economy, its relation to certain other organs, and the effects produced by its removal. Text-books of surgery usually content themselves with a consideration of such conditions as injury, abscess, and tumors of the spleen—well recognized processes which may manifest themselves in the spleen. In addition to these, however, there is an obscure group of conditions in which the spleen appears to be reacting in divers ways to a chronic and long-continued irritant, and with these also the surgeon now finds himself called upon to deal.

THE STRUCTURE AND FUNCTION OF THE SPLEEN

The structure of the spleen is frequently a stumbling block to the student. Broadly considered it may be said to consist of a reticulo-endothelial system so loose in its arrangement that the blood which slowly filters through it is allowed to come into intimate contact with its every part. The branches of the splenic artery end near the periphery by breaking up into terminal twigs, each of which is surrounded by a zone of lymphoid tissue, thus constituting the Malpighian body, an important factory for lymphocytes, which drift outwards and enter the blood sinuses.

The spleen pulp consists of a connective tissue reticulum to which are affixed the pulp cells, often differing from one another considerably in their morphology, but all capable of being grouped together as modified endothelial cells. Some of these cells remain stationary, some wander about in search of food, and others again may proliferate. The pulp cells are collected into cords, between which are the blood sinuses. The blood also runs through the pulp cords, albeit more slowly. The arteries open into the sinuses of the pulp.

The spleen, therefore, is made up of a comparatively small amount of lymphoid tissue and a large number of modified endothelial cells attached to or arising from a connective tissue reticulum. But this reticulo-endothelial structnre is by no means confined to the spleen, for, as Aschoff has pointed out, it may be traced throughout many parts of the body, so that we may speak of a *reticulo-endothelial system*. In other parts where the perivascular connective tissue is open the endothelium will be found to be but loosely attached to the fibrous tissue, and connections are formed between the perithelial and the endothelial cells.

Such an arrangement is seen in most characteristic form in the spleen. In the lymphatic glands a similar arrangement is found, and the endothelial cells are highly phagocytic. The star-cells of Kupffer in the liver, and the meshwork of the bone-marrow, may be included in the same category. All of these cells may be regarded as endothelial in nature, they are highly phagocytic, they contain iron in conditions of blood destruction, and they undergo hypertrophy after splenectomy. All of these structures may harbor micro-organisms or protozoa for considerable periods, malaria in the spleen affording the best example, although syphilis of the same organ may also be cited, and by their continued presence they may give rise to proliferative and fibrotic changes of great significance. The proliferating cells, which will vary with the specialized organ from which they rise, may remain in the organ giving rise to enlargement accompanied perhaps by cirrhosis, or they may enter the blood where they attract the notice of the clinician. To the pathologist the essential basic change is the same whether or not the blood be invaded.

Instead, therefore, of focussing attention upon one organ here or another there and speaking of a series of "diseases" it will probably be more helpful in the future to consider the entire reticulo-endothelial system and the varying ways in which it may react to an irritant.

Pathological changes in the spleen, and indeed in any of the organs belonging to this system, may take two main forms.

1. In the first the irritant produces a local lesion similar to that which may be produced in any other organ. In this way an abscess or a tuberculous nodule may be formed.

2. In the second the irritant, of an essentially chronic character, sets up proliferation or fibrotic changes of an entirely different nature, which may be shared in by other organs of the reticulo-endothelial system.

The effect of such an irritant will vary within wide limits. It may act on the lymphoid cells of the Malpighian bodies causing proliferation of these cells, with the production of the clinical picture of lymphatic leukemia. Or it may act upon the pulp cells, and these may come to function like the cells of the bone-marrow, so that myelocytes are produced, with great enlargement of the spleen, invasion of the blood stream, and the picture of myelogenous leukemia. In Hodgkin's disease there is usually no invasion of the blood, but a bewildering variety of cells may be produced, with fibrosis in the later stages.

In embryonic life the spleen forms both red and white cells, but it loses this power at birth. When unduly stimulated, as in the acute infections and still more in the leukemias, it may regain the power of forming white cells, and may turn out neutrophile leucocytes and their precursors, the myelocytes, in enormous numbers.

It has been suggested that the spleen exerts a controlling and inhibitory influence on the bone-marrow by means of a hormone.

The leucocytosis following splenectomy would be explained by the removal of this control. Hyperactivity of the spleen might cause the leucopenia in typhoid, syphilis, malaria, Banti's disease, Gaucher's disease, etc. It is extremely doubtful, however, if there is sufficient evidence to support this hypothesis of hypersplenism.

Further discussion of this important subject will be found in Sir Berkeley Moynihan's brilliant Bradshaw Lecture, and in that mine of information on all matters pertaining to splenic anemias, R. M. Pearce's The Spleen and Anemia.

The Effects of Splenectomy.—Both in man and in the laboratory animals certain constant effects may be observed after removal of the spleen. The red cells of the blood are diminished in number, but seldom below 3,000,000, and the anemia disappears by the end of two months. A leucocytosis, due mainly to an increase in the number of the polymorphonuclears, persists for about four months. A rise to over 30,000 occurs shortly after the operation, but in a few days time it drops to 20,000.

In animals the fragility of the red cells is found to be decreased, that is to say they are more than usually resistant to the action of hypotonic salt solution. Hemolytic substances produce jaundice less readily than in the normal animal, and it is of interest to note that in pernicious anemia in man the urobilin in the urine, a sure index of hemolytic activity, is diminished after removal of the spleen. It would appear, therefore, that in conditions of hyperactivity of the spleen the organ sensitizes the red cells in some way, sets, as it were, its mark upon them, so that when they arrive at the liver they find in it a premature grave. In animals such as rats there is great diminution in resistance to infectious diseases such as rat plague, and although this has not yet been confirmed in man the possibility must be born in mind.

The cells of the remaining portions of the reticulo-endothelial system undergo proliferation.

Much of the benefit of splenectomy in the several varieties of splenic anemia is probably due, not so much to the removal of injurious substances produced by the spleen, as to the liver being relieved of a large amount of work, so that it is then able to deal with the blood from the spleen which forms 25 per cent of the total amount of portal blood passing through the liver. With the enormous spleens found in disease this amount must be greatly increased. Splenectomy, therefore, will relieve the liver of much of its burden, allowing it to catch up with its work, and preventing or ameliorating the symptoms of liver inadequacy which, sooner or later, are apt to develop.

Enlargement of the Spleen.—The spleen may become enlarged from a variety of causes. Some of these are known, others unknown. Splenomegaly from unknown causes may be accompanied by anemia, and the condition is then often referred to as splenic anemia, an important and vague phrase which should not be taken to signify a disease entity unless it be regarded as synonymous with Banti's disease.

There are in reality many splenic anemias, of which hemolytic jaundice, Banti's disease, etc., are examples. It would be well if the phrase were given up.

The enlargement may be acute or chronic. Acute enlargement (acute splenic tumor) is met with in the acute infectious diseases such as typhoid, pneumonia, septicemia, and ulcerative endocarditis. In the last named septic infarcts may contribute to the enlargement. Abscess of the spleen causes acute enlargement.

Chronic enlargement of the spleen occurs in, (1) leukemia, (2) Banti's disease, (3) Hodgkin's disease, (4) hemolytic jaundice, (5) Gaucher's disease, (6) malaria, (7) kala-azar, (8) syphilis, (9) tuberculosis, (10) amyloid disease, (11) cirrhosis of the liver, (12) mitral valvular disease, (13) sarcoma, (14) echinococcus cysts, (15) thrombosis of the splenic vein, and (16) rarely in pernicious anemia.

A consideration of all these conditions would be outside the scope of the present work, for it is only some of them which bear a relation to surgery.

ACUTE SPLENIC TUMOR

In acute infectious fevers, in septicemia, in acute and subacute endocarditis, and in typhoid fever the spleen is enlarged, and presents the condition known as acute splenic tumor. Two forms may be recognized, the grey or septic spleen and the red or typhoid spleen.

The *septic spleen* occurs in conditions of septicemia. It is enlarged, and so soft that when incised the spleen pulp can be wiped off like paint, or it may even flow. The cut surface has an opaque, pasty appearance, and is of a dull pinkish-gray color. Microscopic examination shows enormous swelling of the pulp at the expense of the blood-sinuses; the pulp-cells are almost all myelocytes or neutrophile leucocytes, evidently produced on the spot in response to the infection. Some of the myelocytes may pass into the blood.

The *typhoid spleen* is very different. It is of a deep red color, and almost jelly-like in consistence. The spleen pulp, instead of containing leucocytes, is packed with red blood cells, which have evidently invaded it from the blood-sinuses. Large numbers of phagocytic cells may be observed containing blood pigment from the broken-down red cells.

LEUKEMIA

Leukemia is a disease which is usually regarded as purely medical, but as surgeons are beginning to remove the spleen in this condition it merits a brief description here.

Leukemia is a disease of the reticulo-endothelial system, the chief organs to be affected being the spleen, the lymphatic glands, and the bone marrow. Two main forms are recognized, the myeloid and the lymphatic, depending upon whether the exciting cause acts upon the reticulo-endothelial cells with the production of myelocytes and neutrophile leucocytes, or upon the lymphoid tissue with the produc-

tion of lymphocytes. In both forms the new cells pass into the blood in enormous numbers. Should they fail to do so the result will be a pseudo-leukemia, and possibly other conditions such as Hodgkin's disease, which differ principally from leukemia in that the new-formed cells remain at the site of origin.

The disease is usually chronic and of several years duration, but the acute lymphatic form may run its course in a few weeks. I have studied the blood from such a case in which the patient, a boy 10 years of age, died 3 weeks after the onset of the symptoms, the first of which was acute inflammation of the throat. An acute myelogenous form is also described in which the cells may be either myelocytes or myeloblasts.

A detailed description of the blood picture would be out of place here. Suffice it to say that in myelogenous leukemia there is a profound anemia together with evidence of hyperactivity of all the blood-forming tissues, so that the leucocytes (every variety) are increased, it may be to 500,000, and myelocytes—both neutrophil and eosinophil—and nucleated red cells are present in the blood. In the lymphatic form the anemia is associated with a lymphocytosis so extreme that the lymphocytes replace all the other white cells of the blood.

In the myelogenous form when the vessels are opened at autopsy the blood in extreme cases may be very thick and of a yellowish-white color, pus-like in short. It was this appearance which first drew Virchow's attention to the condition.

The spleen may be enormously enlarged in myelogenous leukemia, moderately so in the lymphatic form. In the latter there is a general enlargement of the lymphatic glands. The spleen is smooth and firm, and preserves its characteristic shape.

Without going into the histological changes with undue minuteness it may be said that in myelogenous leukemia the reticulo-endothelial cells assume the property of the bone-marrow cells in manufacturing the granular series of leucocytes, and that in consequence the spleen pulp is one mass of myelocytes and polymorphonuclear leucocytes, which overflow and obliterate the Malpighian bodies and compress the blood-sinuses. Similar appearances are seen in the liver and the bone-marrow, the fat of the latter being replaced by a pinkish-grey mass of cells so firm that solid blocks can be cut out. The changes in the marrow and the liver are active, whereas any accumulation of myelocytes in the lymph glands is merely passive, as these glands do not participate in the process.

In the lymphatic form it is the lymphoid tissue which is spurred into excessive activity. The Malpighian bodies overflow into and replace the spleen pulp, and the normal architecture of the lymph glands is completely lost.

What then is the surgical interest of the disease? The cause is unknown, although probably a bacterial or protozal irritant, and the treatment is notoriously unsatisfactory. Splenectomy has been tried on a number of cases, but with a mortality so terrible as to make

the operation unjustifiable. In a series of 51 cases reported in the literature up to Jan. 1, 1918, Giffin estimated the mortality as 93 per cent. The spleen was removed in most of these cases because of its great size.

It is well known that the size of the spleen and the number of leucocytes in the blood may be temporarily reduced almost to normal by certain remedial measures of which benzol, X-rays, and radium are the most powerful. The action of radium on a spleen which may fill the entire abdomen is dramatic in the extreme. Week by week it shrinks, until at the end of two months it may be barely palpable.

W. J. Mayo and his colleagues found that such a reduced spleen might be removed with far greater safety, indeed their mortality is below 4 per cent. Of 26 cases 7 were in good condition after periods of time beyond the life expectancy of the disease. Even if an ultimate cure is not achieved, the patient is relieved of the great discomfort of the huge spleen. Mayo considers that the operation is worthy of further consideration in selected cases.

HODGKIN'S DISEASE

This condition, known also as lymphadenoma, was first described by Hodgkin, pathologist at Guy's Hospital, in 1831. It is characterized by a progressive anemia with enlargement of the spleen, liver, and lymph glands, and therefore belongs to the group of diseases under consideration.

Etiology.—The essential nature of the condition is uncertain, but it may be regarded as a lymphomatosis with granulation tissue formation, involving the reticulo-endothelial system, and may therefore be classed among the infective granulomata. Other views have been and still are held, chief amongst which is that which regards the condition as being neoplastic in nature.

Many suggestions have been made as to the nature of the infecting organism. The tubercle bacillus is accused by some, but this cannot be accepted, although it is true that tuberculosis not infrequently complicates Hodgkin's disease. The work of Fraenkel and Much deserves special notice. These observers treated the enlarged glands with antiformin, and were able to demonstrate granular Gram-positive bacilli which were acid fast. Bunting and Yates attach importance to the presence of a diphtheroid bacillus, to which they have given the name of Corynebacterium Hodgkini, and which they found in the spleen and glands of many cases of Hodgkin's disease. Moreover they claim to have reproduced some features of the disease by injecting this organism into monkeys. Diphtheroid bacilli, however, have so often flashed upon a startled bacteriological world, only to fade away again into the forgotten, that the assumption that they are the causal agents in any disease should always be accepted with grave reserve. These bacteria have been found in the lymph glands in lymphosarcoma and other pathological conditions, and the

general feeling among bacteriologists is that the Corynebacterium Hodgkini is unable to maintain its position.

Clinical features.—The disease is twice as common in men as in women. Young adults are especially susceptible, but many cases occur before the age of ten, and even old age is not exempt. The cervical glands are as a rule the first to be involved, but any glandular group may form the starting point.

In many cases a most remarkable periodic pyrexia is present at some stage of the disease, strongly supporting the infective hypoth-

FIG. 243.—Spleen in Hodgkin's disease showing suet-like areas.

esis. The temperature gradually mounts for 3 or 4 days till it reaches about 105°, remains at that level for another 3 days, and descends to normal in a similar period, only to rise again at the end of 10 days or a fortnight. This sequence may be kept up for long periods of time.

The spleen is enlarged in 75 per cent of cases, and the superficial lymph glands, first one group and then another, become swollen.

In a small number of cases only the deep glands, mediastinal and abdominal, may be enlarged. Rarely the deep glandular enlargement may be unaccompanied by enlargement of the spleen, in which case a correct diagnosis will be next to impossible.

The blood as a rule shows no change beyond the anemia. The proliferating cells remain in the spleen and lymph glands, and do not invade the blood stream. Bunting, however, considers that the presence of transitional leucocytes is characteristic of the disease.

Fig. 244.—Hodgkin's disease. Partly scarred mass in which there are still areas of the characteristic tissue. The large nodule has undergone partial hyaline change. (MacCallum.)

In a case of Byrom Bramwell's which I examined there was an eosinophilia of 30 per cent.

The **gross appearance** of the spleen and the lymphatic glands varies with the stage of the disease. The spleen is moderately enlarged, but seldom attains to the dimensions found in leukemia. Scattered throughout it are characteristic elastic, homogeneous, yel-

lowish-white, suet-like masses which produce against the red background an appearance like porphyry. These masses represent the replacement of the Malpighian bodies by specific tissue to be described immediately.

The lymph glands are enlarged but remain discrete, not matted together as in tuberculosis until the late stages of the disease when they may become fused. They are firm and elastic, and on section have a grey or pale pink, translucent, moist appearance like that of fish-flesh. Running throughout the gland, especially in the later stages, there may be opaque yellow bands of necrotic tissue, or definite scars may be visible on the surface.

The **microscopic appearance** is characteristic, and it is on it that the diagnosis finally depends. Although characteristic, however,

FIG. 245.—Mesenteric glands in Hodgkin's disease. In the fresh specimen the cut surface had a characteristic translucent, moist appearance.

it varies with the stage of the disease, an important point to be remembered.

In the glands the very earliest change is an increase in the lymphocytes, but this is soon replaced by a proliferation of the reticulo-endothelial cells, with the formation of masses of large pale cells with a pale vesicular nucleus.

These cells invade all parts of the gland, and obliterate the normal architecture. Many are so large as to deserve the name of uninuclear giant cells. In addition there are found the most characteristic cells of all, the so-called "lymphadenoma cells" of Dorothy Reed. These are large cells with from four to ten nuclei crowded together and

possessing darkly staining nucleoli. These multinuclear giant cells are probably derived from the uninuclear giant cells, which in turn take their origin from the reticular endothelium. Of particular interest is the presence of eosinophil cells, either polymorphonuclear or uninuclear. Frequently present in large numbers, they are rarely wholly absent, and constitute a valuable feature in determining the diagnosis, for in none of the other pathological conditions affecting the lymph glands are they present in any numbers.

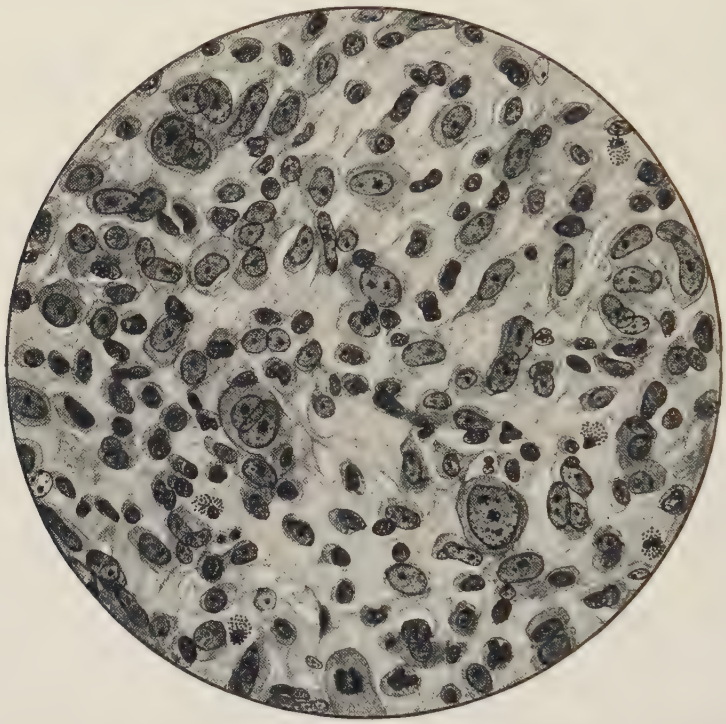

Fig. 246.—Hodgkin's disease; early stage. Marked proliferation of the reticulo-endothelial cells, with a few eosinophils and numerous uninuclear and multinuclear giant cells. (MacCallum.)

In the spleen the changes are similar, and it is this new formation which gives rise to the characteristic grey, elastic, suet-like masses. We may, however, draw this distinction between the changes in the spleen and in the glands. In the spleen the lesions, particularly in the earlier stages, are localized and thus give the naked eye appearance of separate masses, whereas in the glands the lesions are diffuse, so that the cut surface has a homogeneous appearance.

In the later stages a gradual fibrosis replaces the cellular elements, so that dense masses of scar tissue may be seen. Areas of necrosis are frequently present. In a typical case, therefore, the findings are endothelial hyperplasia, giant cells, eosinophils, necrotic patches, and

fibrosis. The microscopic picture will naturally vary greatly with the stage of the disease.

The lesions are not confined to the spleen and the lymph glands. They may be found in any organ where lymphoid tissue with its reticulo-endothelial network is present. This was well exemplified in the following case. A boy, twelve years of age, was admitted to the Winnipeg General Hospital suffering from profound anemia, an enlarged spleen, and an enlarged liver, but no trace of enlargement of the cervical, axillary or inguinal glands. The anemia was of the pernicious type, the blood count being as follows: red cells 1,525,000, hemoglobin 35 per cent, color index 1.14, leucocytes 4,200, polymorphonuclears 49 per cent, lymphocytes 38 per cent, large mononuclears 10 per cent, transitionals 3 per cent, with marked anisocytosis and poikilocytosis, and numerous macrocytes, normoblasts, and megaloblasts. The boy died on the following day. At the autopsy a mass of retroperitoneal glands weighing 160 grams was discovered, there being a smaller mass in the mediastinum. Microscopic changes characteristic of Hodgkin's disease were found in the enlarged glands, the spleen and two accessory spleens, the liver, the thymus, and the bone marrow. In the glands the lesions were diffuse, in the other organs they were discrete. In the liver they were confined to the portal tracts. The changes in the bone marrow may be partly accountable for the peculiar blood picture.

Surgical treatment directed against the spleen is without effect, for it is the lymph glands that bear the brunt of the disease. The enlarged masses of glands may give rise to so much pressure as to necessitate removal. The effect of radiation on Hodgkin's disease is discussed on page 168.

BANTI'S DISEASE

The first thorough study of this disease was made by Banti in 1883, but it was described in 1866 by Griessinger who gave it the name of splenic anemia. The undesirableness of the latter term has already been referred to. Splenic anemia bears a relation to diseases of the blood similar to that which eczema bears to diseases of the skin. It is a rubbish heap from which various distinct entities have by degrees been rescued. Griessinger in his original description included Gaucher's disease, hemolytic jaundice, and Von Jaksch's disease, conditions which are now recognized as being distinct, although doubts are entertained with regard to the last-named.

Enlargement of the spleen with anemia occurs in a number of conditions the cause of which is now recognized; malaria, syphilis, and kala-azar occur as examples. The number of these recognized causes is being continually increased, and the scope of Banti's disease is shrinking accordingly. Moynihan sums up the matter in characteristic fashion: "The group is raided on every side. What remains? Only the forms of splenic anemia, the cause of which is unknown. Or as Mayo wisely and wittingly says: 'Put in the form of an Hibernianism,

incomplete knowledge is essential to the diagnosis. If we know the cause of splenic anemia it is not splenic anemia.' "

The principal symptoms of Banti's disease are, (1) enlargement of the spleen from no known cause, (2) a progressive anemia, (3) a marked tendency to hemorrhage, and (4) portal cirrhosis of the liver with ascites. It is commoner among males, and is a disease of young and middle life. Von Jaksch's anemia in infants may be an infantile form of Banti's disease. It is true that in von Jaksch's anemia a well marked leucocytosis is usually present, but this might be more or less expected in young children. It is by no means certain that von Jaksch's disease deserves to be treated as a separate entity. Banti's disease is remarkably chronic, many cases lasting as long as ten years.

Splenomegaly.—This is the first symptom, and it may be unaccompanied by any other symptom for several years. The enlargement is usually moderate but may be considerable.

Anemia.—The anemia is of the secondary type, with a low red cell count and a low color index. All the formed elements of the blood are diminished in number, so that a leucopenia is a characteristic feature. There may be a relative lymphocytosis, but often the differential count is normal. The spleen may be enlarged for a considerable time before the appearance of the anemia.

Hemorrhages.—Hemorrhages from any of the mucous membranes may occur, but by far the most important form is hematemesis. The vomiting of blood may readily give rise to a mistaken diagnosis of gastric ulcer. Moynihan describes two cases in which three pints of pure blood were vomited within a couple of hours. Robert Hutchison reports a case at the London Hospital in which there were recurring attacks for a period of seventeen years.

Portal Cirrhosis.—In the later stages the liver becomes enlarged, and symptoms of Laënnec's cirrhosis make their appearance. Ascites is present towards the end, completing the fully fledged picture of Banti's disease. Jaundice, if present at all, is only slight.

Banti describes three stages of the disease, although these are by no means clearly differentiated. (1) A stage of enlargement of the spleen and a gradually developing secondary anemia, a stage lasting from 3 to 12 years. (2) A short transition stage in which the liver becomes enlarged, and the patient begins rapidly to go downhill. (3) A terminal stage of atrophy of the liver, ascites, and cachexia, lasting for one or two years. The disease invariably terminates fatally, usually from gastric or intestinal hemorrhage.

Morbid Anatomy.—The spleen is greatly enlarged, but when removed it shrinks and collapses owing to a great escape of blood; the cut surface is flabby, and of a greyish-pink translucent appearance. The chief microscopic change is a fibrosis of the Malpighian bodies spreading out from the central artery, and a general fibrosis of the splenic reticulum with thickening of the trabeculæ and the capsule.

There is often thrombosis of the splenic vein, the walls of which may be atheromatous and calcified. The vein is usually greatly dis-

tended, and there are often huge collateral channels connecting the spleen with the stomach and the diaphragm. The vasa brevia may be represented by great venous channels, which may rupture into the stomach. The danger of this venous enlargement at the time of operation is obvious.

The changes in the liver depend upon the stage of the disease. In the earlier stages it may appear quite normal. Later in the disease it may present the typical appearance of Laënnec's cirrhosis.

The bone marrow is moderately hyperplastic. The lymphatic glands are apparently not involved.

Pathogenesis.—The essential cause of the disease is unknown. Indeed, as has already been pointed out, if the cause of a splenic anemia is known the case can no longer be regarded as one of Banti's disease.

The central fact to be remembered in considering the question of pathogenesis is that removal of the spleen cures the disease. The causal agent, therefore, may either reside in the spleen, or may be so modified by passage through the spleen as to become toxic. Those who support the latter view attribute the enlargement of the spleen to excessive hemolytic activity, but this would not account for the extensive fibrosis which is the most characteristic feature of the histology, nor yet for the fact that there is no increased but rather a decreased fragility of the red blood corpuscles. The presence of a very chronic, hitherto undiscovered, irritant in the spleen acting upon the liver through the portal circulation appears to be the most probable hypothesis.

The explanation of the anemia and of the hemorrhages is likewise difficult. Rolleston considers that the anemia is not primary, but secondary to the hemorrhages. This would not account for the fact that the anemia may develop in cases in which no hemorrhage has occurred. It is more probable that the same agent which produces the fibrosis of the spleen is responsible for the blood destruction.

The hemorrhage is doubtless due in many cases to rupture of the enormously distended vasa brevia into the stomach, aided by torsion or thrombosis of the splenic vein. Such an explanation, however, is not all-sufficient. There is a mysterious relationship between enlargement of the spleen and gastric hemorrhage which is none the less certain. Balfour, in especial, has described cases in which repeated and severe hemorrhages from the stomach, apparently due to gastric ulcer, were completely cured by removal of the spleen, no lesion in the stomach being discovered at the time of operation.

The great surgical interest of Banti's disease lies in the fact that the condition can be cured by splenectomy. The best results are naturally obtained in the early stages of the disease. If the spleen be very large it should first be reduced in size by the application of radium. The average mortality is 10 per cent, but in the late stages it may be as high as 25 per cent. It is remarkable that even with evidence of extensive liver involvement there may be complete recovery when the

source of the trouble is removed, a tribute, as Mayo has pointed out, to the regenerative power of the liver.

HEMOLYTIC JAUNDICE

There is no form of splenic enlargement of greater interest to the surgeon than that associated with the condition known as hemolytic jaundice, because nowhere in all surgery are the results of operation more striking and dramatic. A patient who has been deeply jaundiced for years or since birth may acquire a beautiful white skin within 48 hours after removal of the spleen.

Two main forms of the disease are recognized: (1) the congenital or familial type of Minkowski, (2) the acquired type described by Hayem and Widal. It is still open to doubt as to whether it is justifiable to consider these as two distinct diseases, but a number of facts have been observed which appear to warrant the assumption.

The first type is twice as common as the second. The term familial describes this type better than does congenital, for in a number of cases the disease may develop after birth, but it almost always runs through two or more generations.

Clinical Features.—The symptoms of the two forms are very similar. These are (1) acholuric jaundice, (2) enlargement of the spleen, and (3) anemia. Undue fragility of the red blood cells is a constant feature. Gall stones are present in a large proportion of the cases, and the bile is thick and inspissated. Being acholuric, the *jaundice* differs fundamentally from ordinary obstructive jaundice; there is no bile in the urine although present in abundance in the blood serum, no itching, no bradycardia, and the stools are not clay-colored, but urobilin is present in the urine indicating that there is an increase of hemolytic activity somewhere in the body. In the acquired form acute exacerbations may occur characterized by a rise of temperature, great malaise, a deepening of the jaundice, an increase of the urobilin in the urine, and a temporary increase in the size of the spleen. Such a crisis is undoubtedly due to a sudden increase in hemolytic activity as evidenced by the increase of the urobilin in the urine and the presence in the blood of nucleated red cells and reticulated red cells. Although these crises are supposed to be characteristic of the acquired form, I have seen them in a girl whose sister and brother both suffered from the disease.

The *spleen* is moderately enlarged, but seldom gives rise to great discomfort. It increases in size during the crises, and may at the same time become tender.

The *anemia* is moderate in degree, the red cells varying from two to three million. It is more severe in the acquired form. The anemia is undoubtedly due to the hemolysis which gives rise to the jaundice. The question is, what is the cause of the hemolysis? Some observers such as Minkowski consider that increased hemolytic activity on the part of the spleen offers a complete explanation. Chauffard, however, pointed out that the most characteristic feature of the blood was an

increased fragility of the red blood cells, a diminished resistance to hypotonic salt solution. Both he and Widal maintain that the essential feature of the disease is a dystrophy or weakening of the red cells. In one case which I examined the gall stones which were present contained not a trace of cholesterin, suggesting that there may be a poverty of cholesterin in the protecting envelope of the red blood corpuscles. The improvement which follows removal of the spleen would be quite compatible with such a hypothesis, for a spleen which would do no harm to normal robust red cells would play havoc with such delicate and fragile individuals. In such a case the splenic enlargement would be secondary or spodogenous rather than primary.

Although the two types have so much in common there are certain important points of difference.

The congenital form runs a quieter course. The patient is icteric rather than ill, as Chauffard puts it. Indeed the condition may be so habitual that he consults the doctor about some quite different disease, regarding his jaundice, as Moynihan remarks, with as little interest as the color of his hair. He may be "affected rather than afflicted" by the disease, and may live to an advanced old age. The acquired form, although often quite chronic, is sometimes more eager in its course, it commences as a definite attack of illness, the hemolytic crises are more frequent, and eventually the disease will prove fatal.

The anemia is much more grave in the acquired form, the red cell count in some cases falling as low as 1,000,000, so that the patient is more anemic than jaundiced. Auto-agglutinins are present in the blood in the acquired form, and Widal considers this a proof that the two forms are fundamentally distinct.

Morbid Anatomy.—This presents nothing of interest. The spleen is large and firm, but shows no specific change. The Malpighian bodies appear normal, and the deep congestion of the pulp and blood-sinuses is no more than is found in other diseases of the spleen. Deposits of blood pigment are found in the spleen, liver, kidneys, and bone-marrow.

GAUCHER'S DISEASE

This rare disease was first described by Gaucher in 1882, and was regarded by him as a primitive epithelioma of the spleen. It is characterized by enlargement of the spleen and of the liver, moderate anemia, a peculiar brownish or grayish discoloration of the skin, and the fact that it commences in childhood and that other members of the family are often affected.

The onset is insidious in infancy or childhood, and the disease pursues a very chronic course. It is commoner in females. The enlargement of the spleen may be enormous, greater indeed than is found in any other disease. The anemia is never very severe, but a leucopenia is fairly constant. The enlargement of the liver, which occurs later in the disease, is probably secondary to that of the spleen. Jaundice and ascites are rare.

A characteristic feature is a peculiar brownish discoloration of the skin, which may give rise to the suspicion of Addison's disease. There may also be a yellowish, wedge-shaped thickening of the conjunctiva on both sides of the cornea.

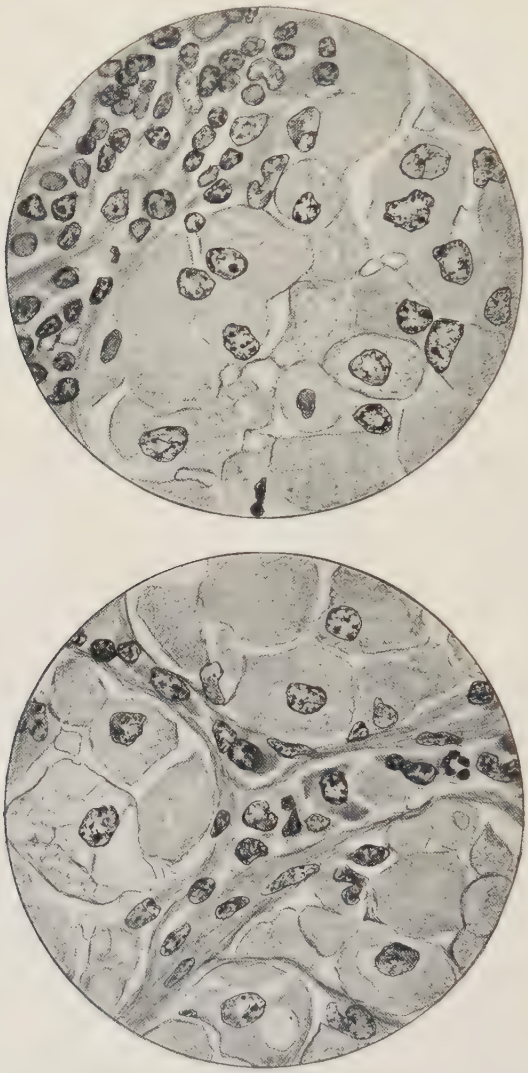

Fig. 247.—Spleen. Gaucher's type of splenomegaly. (Mallory.)

When the anemia has established itself there may be hemorrhages into the skin and mucous membranes. The lymphatic glands may be moderately enlarged, but often they appear normal.

Morbid Anatomy.—Although the real nature of the condition is quite unknown the pathological changes are very characteristic. The enormous spleen is very firm, and on section whitish spots or streaks are seen to be scattered over the grayish-red surface. The splenic enlargement is due to the accumulation of peculiar large vesicular cells with small nuclei, which may be as much as 40 μ in diameter, and which are arranged either in greatly dilated sinuses or as solid masses of cells walled in by connective tissues and presenting an alveolar arrangement. It is these cells which have given the disease the name of large-cell splenomegaly. Recently Anitschkow has shown that a very similar condition may be produced in the spleen and the bone marrow by feeding animals on cholesterin. The clear substance within the cells is probably a lipoid, although it does not give the myelin or fat reactions. In the late stages the cell proliferation is replaced by fibrosis.

It used to be considered that the condition was a tumor formation in the spleen, a kind of endothelioma—for the large cells are endothelial-like in type. Brill and Mandelbaum, however, in a careful study of the disease which should be consulted, showed that similar collections of cells could be found in the lymph glands, the liver, and the bone-marrow. It is possible that these represent secondary growths from the spleen, but it appears much more probable that they are all manifestations of a peculiar reaction of the cells of the reticulo-endothelial system to some form of infection. Further observations are needed, and for the present it would be wiser to say that the nature and cause of the disease are entirely unknown.

Splenectomy has been done in 9 cases with 3 deaths. The operation may give relief from the intolerable burden of the huge spleen, but it can hardly be expected to cure the disease considering how widespread it is. It must be admitted, however, that some cases are still alive a number of years after splenectomy.

PERNICIOUS ANEMIA

Pernicious anemia has not yet become what may be called a surgical disease to an extent which would justify a full discussion of the condition in this place. At the same time recent work is of such a nature as to demand a brief reference to the subject.

The cause of pernicious anemia is still unknown, although it is most probably a chronic infection. Two main factors appear to be at work, or one factor producing two results; (1) increased blood destruction, as evidenced by the presence of blood pigment throughout the reticulo-endothelial system, of urobilin in the urine, etc., and (2) decreased blood formation.

Clinical Features.—Apart from the characteristic blood changes certain general symptoms are usually present. Amongst the most important of these are achlorhydria, glossitis giving rise to a smooth and glossy tongue, pigmentation of the skin, especially on the backs of the hands, attacks of diarrhea and vomiting, and nervous distur-

bances varying from mere tingling sensations in the fingers to symptoms simulating tabes and disseminated sclerosis.

Morbid Anatomy.—The *spleen* is often slightly enlarged. Of 50 spleens which W. J. Mayo removed at operation only 4 were of normal weight. In some instances it was greatly enlarged, weighing as much as 2330 grms., the normal weight being 190 grms. The cut surface, on which the Malpighian bodies can be very plainly seen, may present a rusty tint. Apart from the presence of phagocytic cells in the pulp containing the debris of broken down red corpuscles, the microscopic picture shows little change from the normal.

The *lymph glands* and the lymphoid tissue in general show remarkably little change. The *liver*, cortex of the *kidney*, *heart* muscle, and *lungs* contain a large amount of iron-containing blood pigment (hemosiderin) which gives the Prussian blue reaction with potassium ferrocyanide and weak hydrochloric acid. In the *mouth* glossitis and ulceration of the mucosa may be observed, whilst the *gastric mucosa* is smooth and atrophic.

The *bone-marrow* has the appearance of dark red jelly. It contains great numbers of erythroblasts and megaloblasts, and numerous myelocytes and myeloblasts. In the *spinal cord* areas of degeneration and fibrosis are frequent, especially in the posterior columns.

What relation the spleen bears to the disease is by no means certain. It is assuredly not the *fons et origo* of the condition. It may, however, play a considerable part in the work of blood destruction. For this reason its removal has been advocated in certain cases by W. J. Mayo and others, in conjunction with such measures as blood transfusion and the eradication of foci of infection. Mayo's results up to September 1920 were as follows: 53 cases with 3 deaths; 5 patients living 5 years after operation; 11 patients living 4 years after operation; 22 per cent of patients lived two and a half times as long as the average.

SYPHILITIC SPLENOMEGALY

Enlargement of the spleen with anemia may occasionally be due to syphilis, more particularly in children, in whom syphilis is, next to rickets, the commonest cause of splenomegaly. The condition is of peculiar interest in that it affords an example of a disease which may closely simulate Banti's disease, and which is yet due to a microorganism.

W. J. Mayo has recorded interesting results in a group of syphilitic splenomegalies. The spleen was markedly enlarged, the liver moderately so, anemia was pronounced, and there was a positive Wassermann reaction. Antisyphilitic treatment produced little or no effect on the spleen, on the anemia, or on the Wassermann reaction. It appeared as if the spleen harbored multitudes of spirochetes which could not be reached by arsphenamine. After removal of the spleen the anemia rapidly disappeared, and the other symptoms cleared up under antisyphilitic treatment which previously had been without

effect. Spirochetes were found in the walls of the splenic veins.

Gummata occur but rarely in the spleen, and the usual change in these cases is the diffuse lesion on which Warthin lays so great emphasis.

TUBERCULOSIS OF THE SPLEEN

Healed miliary tubercles are frequently found in the spleen in cases of tuberculosis. Occasionally in general tuberculosis the spleen may be studded with caseous masses of varying size.

FIG. 248.—Tuberculosis of spleen. Specimen removed at operation by Dr. J. Halpenny.

Much more rarely a so-called primary tuberculosis of the spleen may occur. It is hardly conceivable that such an infection can occur without some other tuberculous focus in the body, but sometimes no such focus can be found. There is a specimen in the University of Manitoba Medical Museum of a greatly enlarged spleen removed

by Dr. Halpenny, in which the organ contains numerous large tuberculous masses, and yet no other tuberculous lesion could be found elsewhere. The patient has remained free from any symptoms of tuberculosis for eight years.

MALARIAL SPLENOMEGALY

Malaria is a disease which can usually be treated satisfactorily by medical means. It sometimes happens, however, that patients in whom the spleen is greatly enlarged resist medical treatment in very much the same way as is seen in syphilitic splenomegaly. Jonnesco has reported very gratifying results following removal of the spleen in such cases.

ABSCESS OF THE SPLEEN

This rare condition is usually secondary to some acute infection such as typhoid fever, acute appendicitis, etc. It may be due to direct extension of infection from a subphrenic abscess.

Enlargement of the spleen, chills, and a marked leucocytosis may suggest the correct diagnosis, which may be confirmed by an exploratory puncture.

Although small abscesses are said to be capable of being absorbed, a large abscess demands splenectomy.

CYSTS OF THE SPLEEN

Cysts of the spleen may be: (1) hydatid, (2) dermoid, and (3) simple.

Hydatid cysts are very rare. They may give rise to enormous enlargement of the spleen, which may simulate an ovarian cyst. Suppuration may occur, but frequently the cyst becomes calcified.

Dermoid cysts are of extreme rarity.

Simple cysts may be hemorrhagic or lymphatic. The arteries of the spleen possess no elastic coat and are easily ruptured, with the formation of a hematoma in the spleen pulp. This gives rise to a blood cyst, which is the commonest form of splenic tumor. The cyst is single and may attain a large size.

Lymphatic cysts due to dilatation of lymphatics are multiple and small. They seldom give rise to any symptoms.

TUMORS OF THE SPLEEN

A *cavernous angioma* may very rarely occur. It appears as a dark, soft mass, which consists of a network of blood spaces.

Sarcoma is uncommon. It is more often secondary than primary.

Carcinoma is even rarer. Secondary carcinoma has occasionally been reported, but it is doubtful if there is an undoubted case of primary carcinoma in the literature.

DIFFERENTIAL DIAGNOSIS OF SPLENIC DISEASES ASSOCIATED WITH ANEMIA (MODIFIED AFTER KRUMBHAAR)

Disease	Pathology of spleen	Family history	Time of onset	Duration	Jaundice	Splenomegaly	Anemia	Fragility of red cells	Size of liver	Urobilin
Gaucher's disease.....	Peculiar cell hyperplasia.	Occasionally positive.	Childhood.	Many years.	Rare.	+++	Slight.	Normal.	+	0
Banti's disease.....	Hyperplasia fibrosis.	Negative.	Adult life.	Few years.	Rare.	+	Slight to severe.	Normal.	First + Later −	+
Acquired hemolytic jaundice.	Congestion and pigmentation.	Negative.	Any age.	Many years.	Present.	++	Severe.	Increased.	+ or normal.	+
Familial hemolytic jaundice.	Congestion and pigmentation.	Positive.	Congenital or childhood.	Many years.	Present.	++	Slight.	Increased.	+	+
Pernicious anemia.....	Fibrosis.	Negative.	Adult life.	Few years.	Very rare.	+	Severe.	Diminished.	Normal.	+
Hodgkin's disease.....	Endothelial cell hyperplasia. Giant cells. Fibrosis.	Negative.	Adult life.	Few years.	Absent.	++	Moderate.	Normal.	Normal.	0
V. Jaksch's disease.....	Hyperplasia fibrosis.	Negative.	Infancy.	Several months.	Rare.	++	Slight to severe.	Normal.	+	+

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CHAPTER XXX

THE LYMPHATIC SYSTEM

To the surgeon the lymphatic system is one of the most important in the body, for it is through the lymphatic vessels that bacterial infection passes from the exterior to the interior of the body, and it is through these same channels that the infection marches from one part to another in sepsis, tuberculosis, and carcinoma, while syphilis, although considered a disease of the blood vessels, reaches those vessels by means of the lymphatics. The lymphatic glands, placed here and there in the course of the vessels, and in no sense real glands with an active secretion, constitute one of the most important defense mechanisms in the body, although sometimes they prove woefully inefficient, as in their attempt to destroy carcinoma cells which have been arrested in their interstices. Without these glands death from general infection would be the universal fate. Friedlander in a series of 133 autopsies in children found tuberculous glands in the chest in every case, and but for these glands miliary tuberculosis would have developed in every instance.

The lymphatics commence as blind diverticula from which first a network and then a series of collecting vessels arises. The system is a closed one, and there is no communication by stomata or otherwise, as used to be thought, between the interior of the vessels and the lymph which bathes the tissues; the lymph has to pass through the unbroken wall of endothelium.

In considering the pathology of the lymph glands it is helpful to bear in mind that they are made up of two different tissues: (1) a reticulo-endothelial network composed of a reticulum of fine fibrils to which are attached a peculiar type of endothelial cells (see page 589) and (2) the lymphoid cells which are contained in the meshes of the reticulum. A pathological process may affect the lymphocytes, the reticular fibers, or the endothelial cells, although usually the two latter react together.

Enlargement of the lymph glands may be due to a large variety of causes. The enlargement may be due to bacterial infection, the lymph glands being one of the main mechanisms of defence against such invasion. It may be due to cells of malignant tumors, usually carcinomata, more rarely sarcomata, becoming arrested in the glands and setting up secondary growths. It may be a manifestation of a general blood condition such as leukemia, in which the glands may filter out the blood cells or in which the glands themselves may be the seat of manufacture of such cells. The enlargement may be due to a

general lymphoid hyperplasia in the status lymphaticus. Finally, in many cases the enlargement can be traced to no known cause.

The principal causes of glandular enlargement are: (1) pyogenic infections, (2) tuberculosis, (3) syphilis, (4) carcinoma, (5) Hodgkin's disease, (6) leukemia, (7) pseudo-leukemia, (8) lymphosarcoma, and (9) status lymphaticus.

The lymphatic system is commonly affected by the four great diseases —inflammation, tuberculosis, syphilis, and malignant disease, and when the glands are enlarged these four should first arise to mind, although other less common conditions may also be responsible.

The *preauricular* glands which drain part of the scalp, the eyelids, and the auricle are often affected by tuberculosis. The *submaxillary* glands are frequently the seat of tuberculosis and of epithelioma, and as they drain into the deeper cervical glands the infection may pass into that group. The *submental* glands are frequently infected by epithelioma, but rarely by tuberculosis. The *sternomastoid* glands, situated along the posterior border of the sternomastoid muscle, become enlarged in the second stage of syphilis. The *deep cervical* glands are very often tuberculous, and are often infected from epithelioma of the tongue.

The *supraclavicular* glands are involved in cancer of the breast; those on the left side may also be involved in cancer of the stomach, infection taking place by way of the thoracic duct. The *lateral* or *retropharyngeal* glands may become the seat of suppuration or tuberculous caseation, and may give rise to a retropharyngeal abscess. The *axillary glands* are frequently involved in tuberculosis, cancer of the breast or of the hand, and septic infections of the arm. The *epitrochlear* gland becomes enlarged in syphilis. The *femoral* glands are involved in pyogenic infections of the toes and the sole of the foot. The *superficial inguinal* glands become enlarged in veneral disease and in epithelioma of the genitals. The *bronchial* and *mesenteric* glands are very frequently tuberculous.

LYMPHANGITIS

Inflammation of the lymphatic vessels is due to the entrance of bacteria through a wound or abrasion of the skin which may be so minute as to escape detection. Some of the most serious forms of lymphangitis are due to puncture of a finger at an operation or an autopsy on a septic case. The streptococcus is the usual offending organism.

The inflammation commences in the lymphatic reticulum of the skin, and may spread throughout that reticulum, a spread accompanied by the phenomena of erysipelas, or it may pass rapidly up the collecting vessels to the nearest lymphatic glands, which become swollen, tender, and painful, and in some cases may suppurate. In a superficial infection the inflamed lymphatics are seen as wavy, red lines passing up the limb, but if it is deep these lines need not be looked for, although the part will be swollen and will pit on pressure.

As a rule the inflammation ends in resolution, although suppuration at the site of infection is common. Occasionally a severe infection, arrested at the group of glands into which the lymphatics empty, may set up abscess formation. Should the bacteria pass the line of defence furnished by the glands a general infection will ensue, with pyrexia, chills, delirium, and it may be death.

The changes in the vessels depend on the intensity of the inflammation. In the milder forms the endothelial cells are merely swollen, but as the inflammation becomes more severe the cells are desquamated into the lumen, and clotting of the lymph occurs. Should suppuration supervene the lymphatics become distended with pus, and present the beaded appearance of a rosary. The surrounding tissues are congested, edematous, and infiltrated with leucocytes.

If the inflammation is at all severe the sequel may be connective tissue formation with lymphatic obstruction and the production of a brawny edema. If the obstruction is at all extensive it may give rise to a condition of elephantiasis in one of its various forms.

LYMPHATIC OBSTRUCTION

Obstruction of the lymphatic vessels may be due to a series of causes which may be divided into external and internal.

Of the more important *external* causes may be mentioned pressure by a neoplasm or a mass of carcinomatous glands, pressure due to cicatricial contraction, ligature of a set of lymphatic vessels or extirpation of the corresponding group of glands. A marked example of lymphatic obstruction is sometimes seen in the brawny induration of the arm caused by carcinoma of the breast with involvement of the axillary glands.

Internal obstruction may be caused by the presence of tuberculosis or carcinomatous material in the lumen of the lymphatics. The most serious of all the causes of lymphatic obstruction is the occlusion due to Filaria Bancrofti, the adult form of a nematode worm of which the larval form, the Filaria sanguinis hominis nocturna, is found in the blood in enormous numbers during the hours of sleep. It is not so much the mere presence of the worm that does the damage; it is rather the lymphangitis with subsequent fibrosis and stricture which is the causal agent.

The effects of lymphatic obstruction depend upon the site and the extent of the occlusion. The familiar peau d'orange or pig-skin seen in many cases of superficial breast carcinoma is due, as Sampson Handley has shown, to obstruction of the lymphatics of the skin. Obstruction of the main lymphatic vessels of a limb may give rise, as has already been mentioned, to a brawny edema of the whole limb. If the vessels of the thorax, especially the thoracic duct, be involved they may rupture and lead to a chylo-thorax. In the case of the abdominal vessels a chylous ascites will result. The lymph may be poured into the tunica vaginalis or into the loose tissues of the scrotum, with a resulting scrotal enlargement which may pass belief. The most severe

forms of elephantiasis, in which the legs of the unhappy sufferer may come to resemble those of a young elephant, are almost always due to filarial obstruction.

A peculiar form of lymphatic obstruction to which attention has been directed recently is that known as non-parasitic elephantiasis. It is met with in non-tropical countries, is slow and insidious in onset, and pursues a chronic and painless course. The legs are generally affected, they are white and firm, and not at all tender. Most of the cases have been in women, usually about the age of puberty. The condition must be distinguished from Milroy's disease, an edema of the limbs of a markedly familial character which is as common in

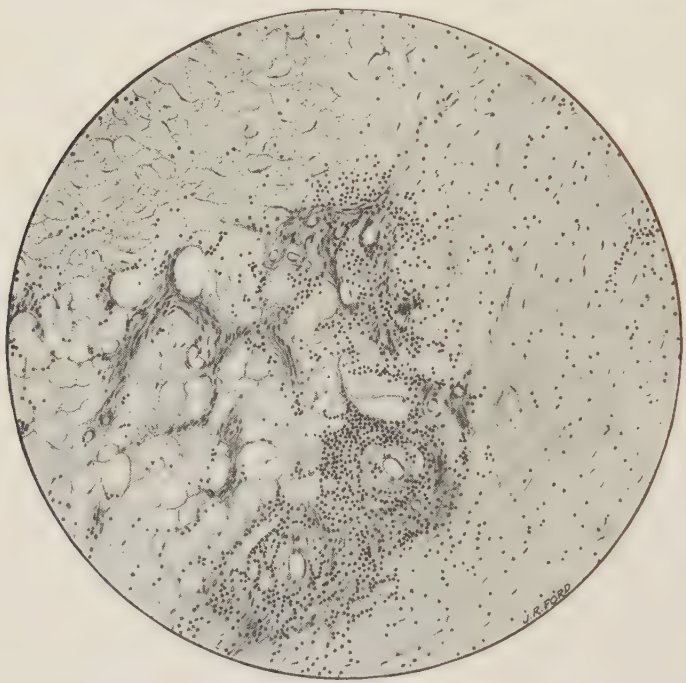

Fig. 249.—Non-parasitic elephantiasis. Perivascular round-cell infiltration and extreme edema in the tissues of the hand of a girl seventeen years of age.

men as in women. In one case of non-parasitic elephantiasis which I had the opportunity of studying recently, microscopic examination showed that there was a distinct chronic inflammatory element in addition to the edema. The patient was a girl seventeen years of age who developed a slow painless enlargement of the hand and wrist, which in the course of eighteen months attained such frightful proportions that the hand had to be amputated. At no time was there any impairment of her general health. The skin and subcutaneous tissue showed an unbelievable degree of swelling and edema, being of a whitish color and having a pale watery appearance. Microscopically the tissue resembled a myxoma, but there were many collections of

small round cells, some of them perivascular in distribution, indicating the action of a chronic irritant. Manson, by the way, does not consider that lymph stasis alone can produce tropical elephantiasis, that is to say a true hypertrophy of the subcutaneous tissue; inflammation is always present in addition in the affected area.

For further information concerning the various forms of lymphatic obstruction, especially those due to the filaria, the very full account by Gerrish in Keen's Surgery should be consulted.

DILATATION OF THE LYMPHATICS

Dilatation of the lymphatics may occur apart from obstruction. This in many cases appears to be a true tumor formation, a lymphangioma, in which there is a formation of new vessels which may be greatly dilated, with the formation of a localized mass. The pathology of lymphangiomas is discussed on page 206.

The lymphatic dilatation may give rise to great swelling of the part affected. A common form of enlargement of the tongue, macroglossia, is of this nature. So also is macrochelia, in which the lip is greatly swollen. These conditions are congenital in origin.

A cystic lymphangioma is a congenital condition in which the lymph vessels of the tumor undergo cystic dilatation. The resultant mass, which is situated beneath the deep fascia, may vary from the size of a fist to that of a child's head, and may project through the fascia under the skin as a thin-walled almost translucent tumor. The condition may persist for a number of years, and may then undergo spontaneous retrogression. This change is usually due to a series of attacks of inflammation which are liable to occur at intervals, and in which the mass becomes red and inflamed with elevation of temperature. Such a condition may be mistaken for an abscess, and on occasion it has been incised, with somewhat disastrous consequences. True suppuration is very rare, but may occasionally occur. The condition is known clinically as a *cystic hygroma*. The most common site is in the anterior triangle of the neck or under the sterno-mastoid. It may also occur in the axilla. If the swelling is punctured with a fine needle a clear serous fluid is obtained.

LYMPHADENITIS

The lymphatic glands being one of the main lines of defense against infection from without, it is but natural that they should frequently be the seat of inflammation, which itself is nothing but a complex defense mechanism. All degrees of inflammation may be encountered depending upon the virulence of the infecting bacteria. Two main forms may be recognized, the acute and the chronic.

Acute Lymphadenitis.—This is usually due to infection of the skin or the mucous membranes. The glands become swollen, painful and tender, and, owing to the periadenitis which is present in all the severer forms, they are matted together. Sometimes it is possible to trace the course of the infection from the primary focus along the red lines of the

inflamed lymphatics. Often, however, the infection appears to pass direct from the initial lesion to the glands, leaving the intervening areas unaffected.

Acute though the inflammation may be, it usually ends in complete resolution. Should the infection be very virulent, and especially if it be due to streptococci, suppuration may occur with abscess formation both in the gland and in the periglandular tissue, with subsequent sloughing of the cellular tissue and of the skin. In these cases the general symptoms will be very marked.

Gross Appearance.—The glands are soft and hyperemic. On section the color varies from gray to pink, and a milky juice can be scraped from the surface. Opaque areas of necrosis may be discernable, more especially in typhoid and diphtheria.

Microscopic Appearance.—Under the microscope the principal change is a great proliferation of the lymphocytes, as evidenced by the presence of numerous mitotic figures in the germinal centers. In typhoid fever, as Mallory was the first to demonstrate, there is a remarkable proliferation of the endothelial cells, which may completely fill up the sinuses. It is to this cellular hyperplasia, whether lymphatic or endothelial, that the enlargement of the gland is mainly due. Hyperemia is usually marked. As the inflammation becomes more severe fibrin is deposited in the lymph-sinuses. This is naturally most marked in pneumonia and diphtheria, diseases in which fibrin formation plays so prominent a part. If the inflammation increases in intensity areas of necrosis may appear, due in part to the cutting off of the blood supply by thrombosis and the pressure produced by the cellular proliferation. Suppuration will be accompanied by the appearance of polymorphonuclear leucocytes which crowd the lymph sinuses.

The *occipital* and *superficial cervical* glands are often infected from pediculosis or wounds of the scalp and the auricle. The *deep cervical* glands are infected from the teeth and mouth, and when suppuration occurs the pus may spread for some distance beneath the deep fascia. The *lateral pharyngeal* glands, infected from the pharynx, may suppurate and give rise to a retropharyngeal abscess. The *axillary* glands are usually infected from superficial wounds or abrasions of the hand, but rarely from septic foci in the deeper structures such as the bones. The *inguinal* glands are infected from wounds of the leg and foot, boils on the buttocks, eczema of the scrotum, or sores on the genitals in the pyogenic venereal diseases, gonorrhea and chancroid.

Chronic Lymphadenitis.—By far the most frequent cause of chronic enlargement of the lymph glands is tuberculosis. Apart from tuberculosis and syphilis, however, there may be a simple chronic lymphadenitis due either to the presence in the gland of staphylococci or streptococci of a low grade of virulence, or to the irritation produced by foreign particles such as dust or carbon. Over 90 per cent of these chronically inflamed glands occur in the neck, affording striking testimony to the important part which infection of the mouth,

tonsils, and teeth plays in the causation of the condition. The inguinal glands may be enlarged in cases of chronic ulceration of the leg. The axillary glands are frequently involved in chronic interstitial mastitis.

The condition may follow on an attack of acute lymphadenitis. In such a case the glandular enlargement may be due to a reparative fibrosis which renders a return to the former size impossible, or it may be due to the infecting organisms, albeit in a state of diminished virulence, making of the gland an abiding home.

Much more frequently, however, the exciting cause must be looked for in some focus of infection in the neighborhood, a focus the removal of which is attended by the disappearance of the glandular enlargement. The most common of these infections are those of the teeth and tonsils. I have seen a case of persistent enlargement of the cervical glands in a boy, in which the possibilities of tuberculosis and Hodgkin's disease were considered, but which proved eventually to be merely due to a seemingly inoffensive chronic pharyngitis.

The glands, although enlarged and hard, are not tender and remain quite discrete, for there is seldom any periadenitis. In the earlier stages the enlargement is due to cellular hyperplasia, the sinuses being filled with proliferated endothelial cells, a condition which may conveniently be named sinus catarrh. At a later date there may be marked thickening of the capsule and trabeculæ with permanent fibrosis.

TUBERCULOUS LYMPHADENITIS

Tuberculosis of the lymph glands is characteristically a disease of childhood, although it may occasionally occur in adults. In children under one year of age the disease usually runs an acute course, but with every succeeding year of life an increasing resistance is established. The glands most commonly involved are the cervical, the bronchial, and the mesenteric.

The bacilli may be carried to the glands in two ways: (1) by the lymph stream, (2) by the blood stream. The distinction is one of practical importance. Lymph spread is by far the more common, and occurs in about 90 per cent of the cases; the primary focus is in the tonsil, nasopharyngeal adenoids, or carious teeth. A clinical distinction of the two groups is possible, because with a blood infection multiple scattered glands are attacked, whereas with a lymph infection the disease remains for a long time confined to one or two adjacent glands. Whatever be thought of operative interference in the lymph spread cases, it is definitely contraindicated in those due to blood spread. In the lymph infections caseation commences at the periphery of the gland, since the lymph stream reaches the gland at that point. In the blood infections it begins at the center, because the main blood vessel passes to the center of the gland before it breaks up.

Herring has shown that colored solutions when injected into the tissues are absorbed by the blood vessels, not by the lymphatics. Insoluble particles, on the other hand, are taken up by phagocytic cells and carried by them into the lymphatics. "The history of the tubercle bacillus in its early stages in the body is identical with that of solid particles such as Indian ink or carmine. A normal physiological process is made use of for the absorption and arrest of the bacillus. The bacillus is carried into the lymphatics by phagocytic cells, and is deposited in the lymphoid tissue of the first lymph gland arrived at. Some of the bacilli appear to be destroyed in the process, others retain their vitality, multiply in the lymphoid tissue, and give rise to a tuberculous focus in the lymph gland. The toxins produced by the action of the bacilli in a lymph gland mix with the lymph stream and set up an intense lymphocytosis in the other glands through which the lymph passes. The toxin precedes the bacilli, and renders the gland less pervious to them by narrowing the lymph sinuses and filling them with lymphocytes." (Herring and Macnaughton.)

Etiology.—The bacilli may be either of the human or the bovine type. The proportion appears to vary considerably in different places. Mitchell found that the bovine bacillus was responsible in 88 per cent of the cases of tuberculous cervical glands in children in Edinburgh, a most remarkable and alarming figure. On examining the Edinburgh milk supply he discovered that 20 per cent of the samples contained tubercle bacilli. English observers have obtained much lower figures for bovine infection. In New York, Park found that only 34 per cent of glandular cases were bovine in type; in children under five years of age, however, 54 per cent of the infections were bovine. It is very desirable that investigations should be carried out in different parts of the country in order to determine the local incidence of bovine infection in children; the results would provide valuable information regarding the state of the milk supply and the prevalence of tuberculous infection in cattle.

The bacilli reach the cervical glands from the mouth, passing through the tonsils en route. It is often stated that the tonsils themselves bear no trace of this passage, just as tubercle bacilli may pass through the wall of the bowel and give rise to glandular tuberculosis without producing a lesion in the intestinal mucosa. Mitchell, however, has shown that tuberculosis of the tonsil is commoner than has been supposed. In 106 cases of tuberculosis of the cervical glands he found microscopic evidence of tuberculosis of the tonsils in 38 per cent of the cases. Even in persons who are apparently healthy tuberculosis of the tonsils can be demonstrated in a considerable number of cases. From a consideration of various large series of figures we may say that in about 5 per cent of individuals evidence of tuberculous infection will be found in the tonsils.

Septic pockets at the roots of teeth is another common source of infection. Tubercle bacilli may be demonstrated in the decayed

root pulps of patients suffering from tuberculous glands in the neck.

An interesting example of the importance of infected milk in the production of tuberculosis of the cervical glands was recently reported by McEachern. A family changed from pasteurized milk to milk supplied by a small herd and sold unpasteurized. Two and a half weeks after the change a swelling appeared in the neck of the youngest child, who was four years of age. Within the following ten days two of the other children developed enlarged cervical glands. In two of the cases the enlarged glands were removed in the Winnipeg Children's Hospital, and I found that they were typical examples of early tuberculosis. The glands of the other child broke down and discharged through sinuses. The herd supplying the milk was tested, and 87 per cent of the cows were found to be tuberculous.

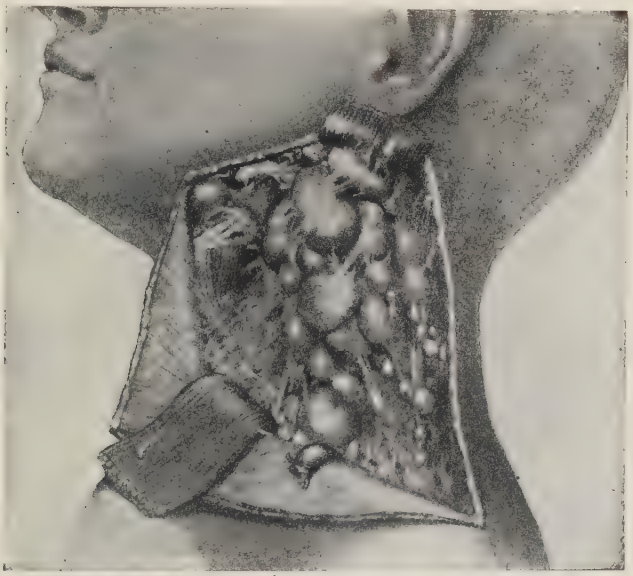

FIG. 250.—Extensive tuberculous involvement of the submastoid, submaxillary, and descending chains. (Dowd.)

Apart, however, from the actual presence of tubercle bacilli in the foci of infection in tonsils or teeth, it is undoubtedly the case that chronic inflammation of these organs opens the path for tuberculous infection to spread to the neighboring lymph glands, a powerful argument for attention to mouth hygiene in children. Other conditions which may be regarded as predisposing to tuberculosis, inasmuch as they open up the portals of infection, are adenoids, middle ear disease, and lesions of the scalp such as impetigo.

The mesenteric glands are infected by bacilli passing through the wall of the bowel, or more rarely from a tuberculous ulcer of the bowel. These bacilli may be contained in tuberculous milk, or in sputum infected from the lungs.

Occasionally the axillary glands may be infected from a tuberculous lesion in the hand, or those in the groin may be infected from the foot.

Clinical Features.—The affected glands are firm and discrete in the early stages before periadenitis has occurred, and to the hand they feel like so many potatoes in a sack. The glands can be readily shelled out. The disease may become arrested at this or almost any subsequent stage. Indeed, with the single exception of the skin, it is doubtful if there is any important tissue affected by tuberculosis in which the outlook is more favorable, provided efficient medical treatment is carried out, than in the case of the lymph glands.

FIG. 251.—A chain of tuberculous glands in the neck removed by operation.

FIG. 252.—Tuberculous cervical lymphatic glands. The glands are largely occupied by yellow homogeneous areas of caseation.

If the disease progresses further periadenitis leads to matting of the glands into one nodular mass. Caseation and softening may occur, with the formation of a cold abscess, or a mixed infection may result in a true suppuration. The abscess makes its way to the surface, destroying the intervening muscles and fascia, and finally ruptures

upon the skin or into an internal cavity. The sinus leading from the gland to the surface is lined by tuberculous granulation tissue, and will usually refuse to heal until that tissue is destroyed. There may be extensive cellulitis with involvement of the skin and the formation of multiple sinuses.

Gross Appearance.—The affected gland is enlarged, sometimes to a great size. On section translucent grayish patches can be seen in the earlier stages, but as the disease advances these become opaque, yellowish, and granular, owing to the occurrence of necrosis and caseation. In the presence of suppuration a creamy, homogeneous, yellow fluid exudes from the cut surface.

Microscopic Appearance.—Under the microscope the early change is seen to be one of proliferation of the lymphocytes and of the endothelial cells lining the sinuses. When caseation has occurred there are large patches of structureless material staining diffusely with eosin, at the margin of which giant cells may be seen. Tubercle bacilli can be stained in the sections. In long standing cases there may be a determined effort to wall in the process by the formation of fibrous tissue. Lime salts may be deposited in the caseous material, a very common occurrence in the bronchial glands. Should healing occur the gland is converted into a mass of fibrous and calcareous material.

Reference must here be made to an uncommon but important variety of gland tuberculosis, known as *chronic hyperplastic tuberculosis.* It is found most frequently in the intestinal canal, but may also occur in the glands. It is because of the resemblance of the microscopic picture to that of Hodgkin's disease that the condition specially deserves notice.

The glands are enlarged and firm, and show no evidence of inflammation. On section they present a gray, translucent appearance, and caseation is absent. Microscopically the brunt of the attack is seen to fall upon the endothelial cells, which proliferate and form small masses, encroaching later upon the rest of the gland. There is no increase in the lymphoid tissue. The picture, therefore, is strongly reminiscent of Hodgkin's disease. Caseation hardly ever occurs.

The condition appears to be a very slow and benign form of tuberculosis. Derval has succeeded in producing a similar condition in rabbits by the injection of attenuated tubercle bacilli.

The outcome of tuberculous lymphadenitis, as has already been observed, is usually a favorable one. Indeed in no form of tuberculosis, with the exception of tuberculosis of the skin, is there so little danger to life. At the same time it is by no means uncommon for the disease to spread from the glands to other and more vital organs. Spread from the bronchial glands to the lung substance constitutes the commonest method of pulmonary infection. Moreover an apparently quiescent gland lesion may through rupture into the blood stream give rise at any time either to a general miliary tuberculosis or to a tuberculous meningitis. A tuberculous gland must be regarded as but a sleeping volcano.

HODGKIN'S DISEASE

Closely allied to tuberculosis of the lymph glands, and in many cases simulating it so closely as to render the diagnosis a matter of considerable difficulty, is the peculiar condition known as lymphadenoma or Hodgkin's disease. The general features of this disease are discussed on page 594, so that it will suffice here to consider only the glandular manifestations.

Clinical Features.—The disease is one of early life, and is much commoner among men than women. Its first manifestation is enlargement of the lymph glands. Several members of one group are involved one after the other, then comes the turn of another group, and so on.

FIG. 253.—Mediastinal Hodgkin's disease invading lung and wall of trachea.

The commonest site is the deep cervical glands, first on one side of the neck and then on the other. The axillary and inguinal groups are also frequently attacked, less commonly the deep glands such as the mediastinal and mesenteric. The spleen, meanwhile, is becoming enlarged, and the anemia and other signs of the disease are manifesting themselves.

The glands are enlarged to a greater extent than in tuberculosis, and are firm, elastic, movable, and quite discrete in the earlier stages, thus differing from the glands in tuberculosis. Later, however, some periadenitis may occur, and they become fused together. Great masses may be formed, which may encircle the neck and compress the trachea and esophagus, interfering with breathing and swallowing.

Such obstruction, however, is more often due to pressure from similar masses in the mediastinum, the presence of which can be detected most readily by means of X-rays. The glands show no tendency to softening or suppuration.

Gross Appearance.—The cut surface of the gland has a moist appearance likened to that of fish-flesh, and it presents the characteristic gray, translucent, elastic areas which represent the formation of the new specific tissue. Later in the disease there may be opaque patches of necrosis, and scarring due to the subsequent fibrosis.

FIG. 254.—Invasion of a rib in a case of Hodgkin's disease of the mediastinal glands.

Microscopic Appearance.—The microscopic changes have been described in discussing the lesions in the spleen (page 597). The gray, translucent, specific tissue is composed mainly of proliferated endothelial cells lining the reticulum, of peculiar giant "lymphadenoma cells," and of eosinophils. In the later stages caseation and fibrosis are added to the picture.

The *relation of Hodgkin's disease to tuberculosis* has been a matter of much debate. Eminent authorities have held that the former condition is merely an atypical manifestation of the latter. It is true that tubercle bacilli have often been demonstrated by cultural methods in the affected glands, but tuberculosis may readily be superadded to Hodgkin's disease. It is also true that, as has been pointed out above, the chronic hyperplastic form of tuberculosis bears a close resemblance to the microscopic picture in lymphadenoma. Nevertheless the evidence is insufficient, and we must conclude that Hodgkin's disease is a distinct clinical and pathological entity in which the reticuloendothelial system reacts in a characteristic manner to some chronic irritant at present unknown.

SYPHILIS OF LYMPHATIC GLANDS

Syphilis, like tuberculosis, has a special predilection for the lymphatic system. It is true that it is usually regarded as a disease of the blood vessels, but it is through the perivascular lymphatics that the spirochetes reach the vessel walls.

The lymph glands may be involved in the primary, secondary, or tertiary stage.

In the primary stage the glands nearest the initial lesion become enlarged a few days after the appearance of the primary sore. The

inguinal glands are those usually involved, but in extra-genital chancre the epitrochlear, the axillary, or the submaxillary glands may be enlarged. The gland is hard and painless, and is sometimes called a bubo. The swelling is never great, but may persist for many months. Suppuration does not occur unless a secondary infection such as chancroid is superadded. The gland is usually swarming with spirochetes. The chief microscopic change is a proliferation of the endothelial cells lining the lymph sinuses. Thickening of the capsule and of the connective tissue septa occurs at a later date.

In the secondary stage a general enlargement of the lymphatic glands throughout the body, owing to the generalized blood infection, is a constant feature. The epitrochlear and the glands along the posterior border of the sterno-mastoid should in particular be examined. The histological changes are the same as those of the primary stage, and spirochetes are present in abundance.

In the tertiary stage gummata may occasionally be formed in the glands, but this is a rare occurrence.

TUMORS OF LYMPHATIC GLANDS

Our knowledge of tumors of the lymph glands is by no means as complete as could be desired. There are many difficulties in the way, one of the chief being that lymph glands react so readily by hyperplasia to the action of a chronic irritant, and such hyperplasia may be indistinguishable from conditions which we regard on other grounds as being true neoplasms. Moreover the relationship of such blood diseases as the leukemias to lymphoid hyperplasia still further adds to the difficulties of the subject.

No attempt will be made here to discuss all the various forms of hyperplasia which may affect the lymph glands. For such a discussion the reader is referred to the chapter on lymphoma and lymphosarcoma in Ewing's Neoplastic Diseases. From the comparatively simple viewpoint of the surgeon we may say that there are three varieties of malignant disease of the lymph glands which merit recognition: (1) carcinoma, (2) sarcoma, and (3) lymphosarcoma.

Carcinoma.—It is said that a primary carcinoma may occur in the lymph glands, but for practical purposes the possibility may be disregarded. Secondary carcinoma, on the other hand, ranks next only to tuberculosis in importance as a glandular disease.

The tumor cells reach the glands from the primary focus by means of the lymphatics. There are two methods by means of which they may accomplish this, by permeation or by embolism. It is difficult to speak with certainty, but the work of Sampson Handley (see page 162) would make it appear that in the majority of cases permeation is the principal factor. The cells permeate or grow along the small and medium sized lymphatics, but when they reach the larger vessels they may well be swept off and carried as emboli to more distant glands. Very much the same process may be observed in vascular thrombosis.

Handley has shown that permeation is an important means of spread in melanotic sarcoma, and that it is as a rule only in the later stages that a general blood infection occurs. Fig. 63 (page 212), drawn from an old man who had suffered from a melanotic sarcoma of the foot for a considerable time, illustrates the gradual extension upwards by permeation of the lymphatics.

The question is not a mere academic one. If permeation plays a part of overwhelming importance in the spread of all carcinomas, then the drastic operative procedures recommended by Handley should be carried out. An illustration providing food for thought is furnished by the case of epithelioma of the hand with enlarged glands in the axilla.

The carcinoma cells first enter the peripheral lymph sinus, gradually permeate the sinuses between the follicles and the cords, and finally wipe away all trace of normal gland architecture. At first the gland may be movable, if no periadenitis due to associated sepsis is present, but soon the tumor cells invade the capsule and penetrate the surrounding parts, giving rise to dense adhesions. The overlying fascia and skin may become destroyed, and a fungating mass appear on the surface.

The structure of the original tumor is reproduced in the gland, be it epithelioma, adenocarcinoma or carcinoma simplex. Indeed not infrequently the secondary growth may be more typical and characteristic than the primary one. It is sometimes difficult to be certain of the nature of a mass in the breast, but the axillary glands may show a typical carcinomatous structure.

It is not known at how early a date the glands may become affected, although cancer in some situations gives rise to metastases much sooner than in others. Glandular involvement, for instance, is very much earlier in cancer of the stomach than in epithelioma of the lip. At the same time it must be admitted that a much earlier diagnosis can be made in the latter than in the former. It is never possible to say that in any case of carcinoma the corresponding glands have not yet become infected. I have seen two cases recently in which a small epithelioma was removed from the hand, only to be followed six months later by the development of a metastasis in the axillary glands.

Sarcoma.—It is doubtful whether a sarcoma of ordinary type occurs in the lymph glands as a primary tumor. Secondary growths are not common, for the spread of sarcoma is mainly by the blood stream. When it does occur the primary growth is said usually to be in the tonsil, the thyroid, or the testicle.

Secondary growths in the glands are frequently formed in melanotic sarcoma, but it is very doubtful whether this tumor should be regarded as a sarcoma at all.

Lymphosarcoma.—Kundrat has separated this tumor from such similar conditions as leukemia, pseudoleukemia, and Hodgkin's disease. In many cases, no sharp line of distinction can be drawn.

The disease begins in one group of glands and spreads to neighboring groups by creeping along the lymphatics. Occasionally

the appearance of secondary growths in distant organs such as the brain, kidneys and skin indicates a true metastasis by the blood stream.

It is remarkably destructive locally, thus differing from leukemia and Hodgkin's disease, and resembling rather one of the infective granulomata, with which it has many points in common. It aggressively attacks the various tissues which it encounters, the capsule of the gland, muscle, periosteum, and bone.

The tumor most commonly commences in the cervical and mediastinal lymph glands. Next in frequency come the retroperitoneal and mesenteric glands, and finally the axillary and inguinal groups. Instead of beginning in a definite group of glands it may first appear in the lymphoid tissue of the pharynx, the stomach, or the intestine.

When the disease starts in the cervical glands it spreads to the wall of the pharynx, the tonsils, and the base of the skull.

Primary involvement of the bronchial glands gives rise to the commonest form of mediastinal tumor, in which the lung and pericardium are invaded, and the patient is strangled by compression of the trachea and bronchi. Many of the mediastinal lymphosarcomas originate in remnants of the thymus gland, and should be regarded as malignant thymomas.

When the retroperitoneal glands are involved the matted glands form a large abdominal tumor, which may compress the veins causing edema, the bile duct causing jaundice, or the thoracic duct causing chylous ascites.

Microscopic Appearance.—In whichever position the disease starts the histological picture is very similar. The normal architecture of the gland is completely wiped out, and replaced by a diffuse mass of lymphocytes lying in a delicate reticulum. The latter feature helps to distinguish the condition from an ordinary round-celled sarcoma.

Two varieties of tumor have been distinguished, one arising from the lymphocytes, the other arising from the reticulum cells. For further discussion on these somewhat recondite matters, Ewing's book must be consulted.

Although lymphosarcoma in its fully fledged form is easy enough to recognize there are atypical varieties in which there must be great uncertainty. The leucocytosis which is frequently present may be so marked as to suggest the possibility of leukemia. Some cases may manifest the endothelial cell hyperplasia characteristic of Hodgkin's disease. And finally masses of lymphoid hyperplasia may be encountered which strongly suggest the possibility of lymphosarcoma, but which never assume malignant characters. Within the last year I have examined an appendix in which the tip was occupied by what appeared to be a solid mass of lymphoid tissue which obliterated the lumen and was beginning to encroach upon the muscular coat. The appearance was very suggestive of malignancy, but the clinical course has been benign.

STATUS LYMPHATICUS

In a discussion of diseases of the lymphatic system which are of interest to the surgeon the peculiar condition known as status lymphaticus or lymphatism deserves mention, for many cases of death under anesthesia are due to this cause.

The condition presents the following characteristics:

1. Both in children and in adults sudden death may result from an apparent trivial cause such as a slight blow, mild anesthesia, etc. In some cases no cause can be discovered.

2. There is a general hyperplasia of the lymphoid tissue throughout the body. The lymph glands are all enlarged, and so also are the spleen and the lymphoid tissue in the pharynx and intestine.

3. The thymus is said to be invariably enlarged, so that the condition is sometimes called status thymicolymphaticus, and the death is known as thymic death. As is pointed out in the next section, the work of Hammar and others has thrown grave doubt on the supposed relationship between enlargement of the thymus and true thymic death, although the enlarged thymus may be responsible for fatal compression of the trachea in thymic asthma.

4. There is a hypoplasia and narrowing of the vascular system. Cerebral hemorrhage in young non-syphilitic subjects may be associated with status lymphaticus, and is probably due to the vascular weakness. Death is a cardiac one, the heart giving out as though from an advanced organic lesion.

5. In patients suffering from this condition there is usually a characteristic type of constitution, described by Riesman in the Oxford Medicine in the following words. "The child is slender, graceful, delicately moulded (the angelic child), and blue or brown-eyed, with transparent skin and soft hair. The adult has the same general features; he is slender, well proportioned, and narrow waisted. The hair of the chest and the axilla is scanty. The pubic hair does not grow up towards the umbilicus, but ends in a sharp, transverse line above the pubes (transverse crines) as in the female."

THE THYMUS

The thymus gland may be regarded as a portion of the lymphatic system. It consists, however, of two entirely different tissues, different in origin, in structure, and probably in function. These tissues are (1) the epithelial cells, derived from the fourth branchial cleft, which constitute the medulla of the gland where they are collected in the aggregations known as Hassal's corpuscles and are also found in the cortex as the reticular cells, and (2) the lymphoid cells which make up the greater part of the cortex. The thymus is essentially an epithelial organ infiltrated by lymphocytes.

At birth it weighs 13 grams, gradually increases in size till the age of puberty when it weighs about 35 grams, and from that period

onwards undergoes a gradual atrophy. It continues, however, to function actively throughout life.

The thymus is never found in a normal condition in persons who have died from disease, for it responds with great readiness to hostile influences, and the cortex becomes greatly reduced by increased emigration of lymphocytes, so that the entire gland may be only one hundredth of the normal weight. As a result of this shrinkage of the lymphoid tissue there may be a relative increase in the number of the Hassal corpuscles which is more apparent than real. An erroneous idea of the normal size of the thyroid is therefore obtained at autopsy, and in cases of sudden death the unaltered thymus may *appear* to be unduly large. This accidental involution is produced not only by the majority of diseases but also by other influences such as inanition, pregnancy, and X-ray treatment.

Hammar of Upsala in a series of studies on the thymus has shown that there may be a true increase in the epithelial cells and the Hassal corpuscles, even though the bulk of the gland is diminished. This increase takes place in response to the introduction of any antigenic toxin into the body, and it can be particularly well demonstrated in the case of diphtheria toxin and snake venom. It would appear that the function of the epithelial cells may possibly be antitoxic nature.

Thymus Hyperplasia.—Hyperplasia of the thymus is frequently found in Graves' disease, in the so-called thymic death, and in a number of other conditions of less importance, such as Addison's disease, myasthenia, acromegaly, and castration. In *Graves' disease* there is a great increase of the lymphoid tissue of the cortex which is apparently merely one manifestation of the general lymphoid hyperplasia found throughout the body. The Hassal corpuscles may also show a marked hyperplasia. There is thus a definite increase in both of the thymic tissues, an increase which is also observed when an animal is fed on thyroid gland. The Hassal corpuscles may also show a marked hyperplasia.

Thymic death is a term which includes two quite different conditions. The first is thymic asthma, characterized by inspiratory dyspnea; it is caused by pressure of the enlarged thymus on the trachea, and death takes place from suffocation. The second is the true mors thymica, in which there is no difficulty in respiration, and death may occur quite suddenly and unexpectedly in an apoplectiform manner, it may be during sleep, due apparently to heart failure. From a microscopic study of 37 of these cases in children Hammar came to the conclusion that the thymus was not directly concerned with the cause of death, and that the apparently large size was due to the absence of accidental involution.

Tumors of the Thymus.—The only tumor of any importance is that known as the thymoma, and even it must be considered a rarity. Much confusion exists as to its true nature, and several varieties have been described. Two main types may be distinguished: (1) malignant thymoma or lymphosarcoma, and (2) carcinoma.

The *malignant thymoma* resembles in structure a lymphosarcoma, but careful examination will reveal differences. The cells are larger than those of the typical lymphosarcoma, large pale cells recalling those of Hodgkin's disease may be seen, and occasionally giant cells are present. Although it is commonly thought that the cells are derived from the lymphoid cells of the gland, Ewing and others consider that they originate from the reticulum cells.

The carcinomatous type is composed of masses of pavement or cubical epithelium, with concentric layers of cells resembling Hassal's corpuscles. The tumor probably arises from the epithelial elements of the gland.

Both of these tumors are highly malignant. They compress and invade the surrounding structures, and may extend downwards as far as the diaphragm. The bronchial, cervical, and axillary glands become involved. A thymoma forms one variety of mediastinal tumor. Metastasis to distant organs sometimes occurs.

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CHAPTER XXXI

THE CRANIUM AND ITS CONTENTS

Before considering the cranium, the brain, and the meninges, a few words may be devoted to the scalp.

THE SCALP

The scalp is subject to the same diseases as the skin in other situations. It presents, however, one or two anatomical peculiarities which have a bearing on the pathological processes to which it is liable. The skin is bound to the epicranial aponeurosis of the occipito-frontalis muscle by dense fibrous tissue in which run the vessels which supply the scalp, and with which the outer coat of these vessels is continuous, so that when cut they are unable to retract. It follows, therefore, that when an artery is divided the bleeding is apt to be very persistent.

The vascular supply of the scalp is extremely abundant, so that it is very rare for a portion, however badly damaged, to die. For this reason the surgery following injuries can be conservative in the extreme, and no portion of the scalp, however hopeless it looks, should be sacrificed.

Very free communications exist between the veins of the scalp and the intracranial venous sinuses by means of the emissary veins which pass inwards through the skull, and which may be the ready means of conveying infection to the interior of the cranium. Every wound of the scalp carries with it possibilities of future mischief unless all bacteria are carefully excluded.

Finally, the connective tissue between the aponeurosis of the occipito-frontalis and the cranium is so loose that it offers no resistance to the spread of blood from a bleeding vessel. A large blood tumor may thus be formed, which is known as a subaponeurotic cephalhematoma. In some cases the blood may be poured out beneath the pericranium, with the formation of a subpericranial cephalhematoma. The latter is naturally bounded by the limits of the bone to which the pericranium is attached, the former is irregular in shape, and may be only limited in size by the attachment of the occipito-frontalis itself. This form of hemorrhage is often due to the use of instruments during delivery.

Of the diseases of more particular interest affecting the scalp may be mentioned wens, dermoid cysts, sebaceous adenoma, cirsoid aneurism, and plexiform neuroma.

Wens are sebaceous cysts of the scalp, with little or no hairy covering, frequently multiple, and usually occurring in the later years of life.

Dermoid cysts, being congenital in nature, are met with in childhood. They are commonest over the anterior fontanelle and the occipital protuberance.

Adenoma of the sebaceous glands is a rare condition, but apt to be puzzling unless its presence is kept in mind. It forms a solid mass with a very thin covering of skin. One specimen in the University of Manitoba Pathological Museum is as large as a medium-sized potato.

A cirsoid aneurism forms a mass like a bag of worms. It is made up of a great number of tortuous, dilated, pulsating vessels, and is in no sense a true aneurism. The patient's chief complaint is of a rushing noise in the head.

A plexiform neuroma, affecting the branches of the fifth nerve, occurs as a diffuse soft mass in which separate cords can be made out. Other forms of neurofibromatosis may also be met with in the scalp.

DISEASES OF THE CRANIAL BONES

The chief pathological conditions affecting the cranial bones are the usual four, inflammation, tuberculosis, syphilis, and tumors.

Osteomyelitis.—Osteomyelitis of the cranial bones differs from that seen in other bones in that it is much more frequently secondary to wounds of the scalp, infected fractures, middle ear disease, etc., than primary in origin. This is due to the absence of the vascular epiphyses and metaphysis which are so frequently the seat of infection in the long bones.

The inflammation when derived from the outside affects principally the outer table; when primary in the bone it commences in the diploe and spreads outwards. The sequestrum produced is, therefore, as a rule quite superficial. A very long time is occupied in its separation, and there is remarkably little new bone formation, so that if there is a large bony defect it remains largely unfilled.

The inflammation may spread to the dura causing a subdural abscess, to the pia-arachnoid causing a septic meningitis, or to the cranial sinuses causing a sinus phlebitis. When an abscess forms between the dura mater and the bone the overlying skin becomes swollen and edematous, the condition known as *"Pott's puffy tumor,"* which will be alluded to again presently. It indicates not only the position of the inflammation, but to some degree its extent.

Tuberculosis.—Tuberculous disease is commoner among children and adolescents than among adults. The bones most frequently attacked are the frontal and parietal; much less frequently the temporal and occipital. Two forms of the disease are usually described, the perforating form and the diffuse progressive infiltration. This distinction has broken down, and it is probable, as Valentine St. John puts it, that there is but one form of tuberculosis of the cranial vault, circumscribed in the early stage and diffuse in the later.

The disease commences in the loose tissue of the diploe, through which it spreads, attacking here and there the tables of the skull. Both tables may be attacked at the same point, with the resulting for-

mation of a sequestrum involving the whole thickness of the bone. Or the outer table may be destroyed and a cold abscess formed, which at first lies between the pericranium and the bone, but later perforates the pericranium and comes to occupy the loose tissue of the scalp. Finally, the disease may extend inwards, the inner table is perforated, and the dura exposed. A pachymeningitis is the natural result, but a true tuberculous meningitis is a rare complication, owing perhaps to the thickening of the dura. Moreover it is very unusual for a cold extradural abscess to form in situ, although pus may make its way from the outside of the skull through the opening in both tables, and thus reach the interior of the cranium.

It is sometimes stated that tuberculosis destroys the inner table to such a greater extent than the outer that the area of erosion becomes funnel-shaped with the mouth of the funnel looking inwards, but this is not sufficiently constant to be of any diagnostic value. The perforation in the outer table may be single or multiple; as many as 29 perforations have been found in the skull of a child.

Syphilis.—The only important syphilitic manifestation in the cranium is the gumma. A gumma forms a painless, elastic swelling which may be mistaken for a sarcoma, a subperiosteal abscess, or a cold abscess. Although the gumma is painless to the touch, syphilitic osteitis is usually accompanied by pain, sometimes of a very severe nature, and characteristically worse at night.

Unless infected the separation of the necrosed portion occupies a very long time. Infection, however, is very liable to occur, and necrosis is then much more rapid and extensive, so that a macerated specimen will show the widespread worm-eaten appearance so frequently seen in museums. It is the outer table which is principally affected, although the inner table may be involved to a lesser extent. The mouth of the funnel in this case will be directed outwards. If several gummata are present the necrosed bone presents the appearance of intersecting circles, and large sequestra may be formed which on separating leave correspondingly large defects in the skull.

The lesions of syphilis differ from those of osteomyelitis and tuberculosis in that they are accompanied by a considerable amount of bony overgrowth. When healing occurs, therefore, a depressed scar is left with definitely raised bony edges.

Tumors.—*Osteoma* of the skull has already been described on page 179.

Sarcoma.—A sarcoma usually arises in the periosteum, but it grows rapidly and may soon penetrate to the interior of the cranium. It forms a soft, diffuse swelling which may be mistaken for a gumma or an abscess. The prognosis could not be worse.

Secondary Tumors.—Metastases in bone, and particularly in the cranium and spine, are for some unknown reason peculiarly apt to occur in carcinoma of the thyroid, the breast, the prostate, and in hypernephroma. The growths may be single or multiple, and frequently lead to errors in diagnosis.

CONCUSSION OF THE BRAIN

Concussion is a condition of immediate and widespread loss of cerebral function following upon a blow on the head. The fact that the loss is both immediate and widespread is of great importance in determining the exact pathology of the condition.

Clinical Features.—The patient passes instantaneously into a state of profound shock in which both the higher faculties and the vital functions are so perilously suspended that he may appear to be on the very brink of death; yet recovery may be not only spontaneous but fairly speedy, although in many cases it is a much more long-drawn-out process. Consciousness is lost instantly, the patient falls like a log, is pale as death, and covered with a cold clammy sweat. The temperature drops away below normal, the pulse is imperceptible, the respiration almost suspended. After a varying period a stage of reaction sets in, the temperature rises, the pulse beomes full and bounding. Recovery may be rapid, or the patient may manifest symptoms of profound irritability ("cerebral irritation") in which, as Erickson says, "it appears as if the temper, as much as or more than the intellect, were affected." These clinical considerations are necessary for a discussion of the difficult subject of the pathology of concussion.

Pathology.—The pathology of the condition is complicated by the fact that the autopsy findings are extremely variable. These may be divided into three groups.

1. There may be laceration of the brain, especially involving the under surface of the frontal lobe and the under surface of the temporosphenoidal lobe, owing to the rough nature of the orbital plate of the frontal bone and of the petrous temporal. Accompanying the laceration there is a varying amount of hemorrhage which, if the pia be torn, will enter the subarachnoid space and appear in the cerebrospinal fluid.

2. There may be minute petechial hemorrhages scattered throughout the brain, which may only be visible on microscopical examination. Such lesions were not infrequently found during the war in men who had been killed by the bursting of a high-explosive shell, but in whom no other gross lesions could be detected.

3. In a smaller number of cases no lesion of any kind can be found in the brain. In such cases the cause of death may be found in the spinal cord. Bowlby mentions two cases of men suffering apparently from concussion after blows on the head in whom the autopsy revealed no lesion of the brain, but fracture of the spine high up with laceration of the cord.

What, then, is the relation of these varied lesions to the fairly constant clinical picture of concussion? It is more than probable that they bear no relation to the immediate condition of concussion, although they may materially modify the subsequent course.

Numberless theories have been advanced to explain the phenomena of concussion. The "molecular commotion" which used to be so glibly adduced is nothing but an example of one of those meaningless phrases

which have so often served to delay the advance of medical knowledge by casting a veil of convenient obscurity over the facts which demand explanation.

The cause of concussion must be instantaneous and widespread. The only factor which appears to meet the demands of the situation is cerebral anemia. The skull is not the rigid incompressable structure which it is apt to appear. It may exhibit a remarkable degree of elasticity when subjected to pressure. The result of a blow is to produce a bending inward of the bone which in turn causes momentary but severe compression of the brain, so that the vessels in every part of the brain, medulla as well as cerebrum, are emptied, and a profound degree of cerebral anemia is produced. It may be, as Duret has suggested, that the cerebrospinal fluid is driven out of the lateral ventricles into the fourth ventricle with such force that it paralyses the cardiac and respiratory centers in the floor of that ventricle. This, however, is probably a factor of only secondary importance. The extensions of the subarachnoid space which, as will be shown presently, accompany the vessels into the depths of the brain and are filled with cerebrospinal fluid, feel the force of the fluid wave, and, by giving way, may give rise to the minute petechial lesions already referred to.

The subsequent reaction is due to a refilling of the vessels, and the further clinical course will no doubt be largely influenced by the concomitant lesions present. The minute ecchymoses would not of themselves be sufficient to produce the train of symptoms such as headache, restlessness, and clouding of the mind which so frequently follow concussion, but they excite an inflammatory edema in their vicinity which is enough to give rise to a slight general cerebral edema and heightened intracranial pressure, with the series of disturbances which usually accompany that condition.

COMPRESSION OF THE BRAIN

There is no organ in the body in which the effects of pressure are so serious as in the brain, owing to the fact that it is confined in a bony case incapable of expansion. It is true that a certain amount of elbow-room may be afforded by the flow of the cerebrospinal fluid from the cranial into the spinal cavity, but this is comparatively limited in amount, and affords greater relief in the acute compression accompanying a blow on the head than in the more chronic conditions about to be discussed.

Etiology.—Compression of the brain is produced by anything which will cause a rise of intracranial tension. The chief causes are (1) intracranial hemorrhage, (2) abscess, (3) tumor, and (4) edema. The pressure of a depressed fragment of bone, the presence of a foreign body such as a bullet or a piece of shell within the brain, if they give rise to compression at all do so by virtue of the inflammatory edema which they induce. Edema, indeed, is one of the most important causes of compression.

Effects.—The effects are usually both local and general, although in such a condition as hydrocephalus (which may be taken for the moment as an edema of the ventricles), they are only general. At the seat of pressure the vessels are emptied of blood, whereas the vessels of the rest of the brain tend to be dilated, all parts, however, suffering in their nutrition. The cerebrospinal fluid is driven as much as possible into the spinal canal. The pressure then begins to affect the brain substance. The convolutions may be greatly flattened, a condition seen in its most extreme form in internal hydrocephalus. The higher centers suffer first, so that consciousness is clouded and finally lost. Pressure on the motor areas will first cause irritation with convulsive movements, followed later by paralysis. The vagus and vaso-motor centers in the medulla are stimulated; the pulse, therefore, is slow and the blood pressure raised. Finally all the irritation phenomena are replaced by those of paralysis.

Edema of the Brain.—Edema is the commonest complication of all intracranial lesions, whether they be hemorrhage, inflammation, or new growth. It may be merely a part of a general edema, or due to some constitutional disturbance, as in uremia and the "wet brain" of alcoholism.

Traumatic cerebral edema is a condition of the greatest importance. It occurs as a more or less serious complication in 95 per cent of all severe head injuries, whether or not there has been fracture of the skull. Fracture of the base of the skull proves fatal because of the edema and hemorrhage which accompany it; the mere fracture is of little importance.

The edema in the first instance is comparable with the edema which follows trauma in any part of the body, and is of a true inflammatory character. Soon, however, an edema of an entirely different nature develops; it is this which endangers the life of the patient, and it is due to interference with the circulation of the cerebrospinal fluid.

The mode of production and absorption of the cerebrospinal fluid is considered in detail in the next section. Suffice it to say here that in the main the fluid is produced within the ventricles by the choroid plexus, escapes into the subarachnoid space through the roof of the fourth ventricle, and passes up over the brain stem to be absorbed from the cerebral subarachnoid space into the superior longitudinal sinus. Anything which tends to obliterate that space and interfere with the absorption will inevitably result in stasis of the cerebrospinal fluid and a general cerebral edema.

As a result of some form of trauma a local swelling of the brain soon appears at the site of injury, and reaches its maximum in from 24 to 48 hours. If the local swelling is only moderate in degree the interference with the absorption of the cerebrospinal fluid will be correspondingly slight, and the parts will return to normal in the course of a few days, although during that time the intracranial pressure remains raised.

If, however, the local swelling is more marked, the general effects will be the more serious. The brain is contained in a rigid, inexpand-

able box, and the only compensatory mechanism to counteract the increased pressure is the outflow of cerebrospinal fluid into the spinal canal. As the local swelling increases, the cerebrospinal fluid is driven out of the cerebral subarachnoid space into the corresponding space in the spinal canal, the brain is pressed against the vault of the skull, the subarachnoid space is compressed and obliterated, and the absorption of cerebrospinal fluid from that space stops completely. Circulation of the fluid ceases and stasis results. Meanwhile the choroid plexus continues to secrete cerebrospinal fluid, although perhaps more slowly, and the accumulating fluid in the basal cisterns pushes the brain still more forcibly against the cranial vault, still more effectually interfering with absorption. As the brain is pushed upward the brain stem tends to plug the narrow incisura tentorii, so that the fluid accumulates in the basal cisterns and distends the ventricles, producing a form of communicating hydrocephalus which is considered more fully in the section on hydrocephalus. The dilatation of the ventricles aggravates a situation which is already sufficiently hopeless, and pressure on the medulla develops, with death as the result.

At autopsy the dura is very tense, the convolutions are markedly flattened, and the sulci can be traced with difficulty. In the traumatic cases there is none of the great accumulation of fluid in the subarachnoid space over the cerebrum which is seen in the wet brain of alcoholism. The cut surface of the brain, however, is wet and pale, and a clear fluid exudes from it. The differentiation between grey and white matter is much less marked than usual. The brain, in short, is water-logged. The fluid in the perivascular spaces, which may be regarded as the lymph of the brain, is unable to escape into the subarachnoid space owing to the high cerebrospinal fluid pressure, and is therefore imprisoned within the brain. Microscopically the cortical cells show marked degeneration, and are widely separated by the edematous fluid, which also distends the perivascular lymph channels.

A subtemporal decompression merely allows any fluid already imprisoned in the subarachnoid space to gush out, and the brain then blocks the opening, thus effectually preventing any further escape of fluid. It is obvious that unless the vicious circle be broken by relieving the pressure below the tentorium by lumbar puncture there can only be one termination. The lumbar puncture should be done at the earliest possible moment and not delayed until symptoms of extreme pressure have developed, for the pressure on the brain speedily leads to anemia, which in turn is followed by destruction of tissue and gliosis. This is probably the chief cause of the late effects commonly known as traumatic neurosis. The danger of the medulla being forced into the foramen magnum, which is undoubtedly great in cases of brain tumor and which is frequently attended by fatal results, need not be feared in traumatic edema.

The pressure of the cerebrospinal fluid, which normally varies between 7 and 9 m.m. of mercury, rises to from 25 to 50 m.m.

This great rise of pressure may be present as early as 6 hours after the injury.

Effect of Injection of Hypertonic Salt Solution.—The recent work of Weed and McKibben on the effect on brain volume of injections of hypertonic saline solution is of great interest in relation to cerebral edema whether due to trauma or to general constitutional causes. These workers found that the experimental intravenous injection of hypotonic solution such as water was followed by a marked swelling of the brain, so that when an opening is made in the skull the brain will herniate out for a distance of several millimeters. On the other hand when hypertonic solutions such as 30 per cent sodium chloride or saturated sodium bicarbonate are used there is a marked decrease in the bulk of the brain, and when the skull is opened it will be seen to fall away several millimeters from the surface of the skull. There is a corresponding diminution in the pressure of the cerebrospinal fluid. The explanation of this remarkable diminution in the volume of the brain is to be found in the increased osmotic pressure within the blood vessels, as a result of which the cerebrospinal fluid is drained into the blood stream. Moreover, Weed has shown that whereas normally the cerebrospinal fluid is absorbed into the great venous sinuses, after the injection of hypertonic salines absorption also takes place through the ependymal lining of the cerebral ventricles and also by way of the perivascular lymph channels.

It might be thought that the shrinkage in the brain bulk would be accompanied by a corresponding decrease in the ventricular spaces. Austmann and Moorhouse, working in the department of physiology of the University of Manitoba, have shown recently that the reverse is the case. By the ingenious method of utilizing the temperature of a Manitoba winter so that the head of the animal could be rapidly frozen after the injection of hypertonic saline, and then making sections through the skull and brain, they were able to demonstrate that the ventricles, instead of being collapsed, were widely dilated. This dilatation of the ventricles was evidently purely compensatory and the results offer some interesting suggestions as to the possible function of the ventricles. It may be mentioned in passing that Austmann and Moorhouse found that the normal ventricles in the dog are largely potential cavities, the walls being mostly in apposition except in the lateral ventricles where the roof is separated from the floor by a layer of cerebrospinal fluid from 2 to 4 m.m. in depth.

Foley, in a recent experimental investigation, confirms the observation that the fluid may be absorbed through the ependyma, and also through the capillaries of the brain substance with reversal of fluid flow in the perivascular spaces. One of his most interesting observations was that the altered absorption causes changes in the grosser currents of the fluid. The current of fluid in the aqueduct of Sylvius is completely reversed, a retrograde flow from the subarachnoid space to the lateral ventricles being established.

THE CEREBROSPINAL FLUID

Before passing to the subject of hydrocephalus a short review of the methods of production and absorption of the cerebrospinal fluid will be necessary, and a brief reference will be made to the functions of the fluid and its behavior under pathological conditions. An examination of the cerebrospinal fluid is of enormous value in arriving at a correct conception of what is transpiring within the cranial cavity, for the fluid is the sensitive mirror in which is reflected many a tell-tale picture of cerebral disease.

The cerebrospinal fluid is contained in the ventricles of the brain and in the subarachnoid space. In the cranial cavity two spaces may be recognized, the subdural between the dura and the arachnoid, and the subarachnoid between the arachnoid and the pia. It is curious that there is no communication between these two, so that not only an extradural hemorrhage but even a hemorrhage into the subdural space may show no blood in the spinal fluid. Often, however, the arachnoid is torn by the initial injury, so that in a fracture of the skull with middle meningeal hemorrhage the discovery of blood at lumbar puncture may be of great diagnostic importance. The possibility of the blood being due to the puncture must always be kept in mind. The method of differentiating pathological from puncture hemorrhage is given on page 640.

The fluid is *secreted* in the lateral ventricles and the third ventricle by the choroid plexus, passes along the aqueduct of Sylvius to the fourth ventricle, and escapes thence into the cerebral subarachnoid space through the small openings in the membranous roof of the ventricle—the median foramen of Magendie and the two lateral foramina of Luschka.

The arachnoid clothes the brain much in the same way that a mit covers the hand; it does not adapt itself closely to the convolutions, nor dip down into the fissures. The pia, on the other hand, may be compared to a closely fitting glove, which adapts itself to every fold and fissure of the organ.

The *subarachnoid space*, which over the upper part of the brain is of the narrowest dimensions, widens out into cavernous cisterns at the base. It is into these cisterns that the fluid is poured from the fourth ventricle, and it passes forward and upward under the medulla, pons, and mid-brain in a manner which will be described more in detail in discussing the production of hydrocephalus. The spinal is continuous with the cerebral subarachnoid space, and passes downwards as far as the last lumbar vertebra. As the spinal cord ends at the lower border of the first lumbar vertebra the cerebrospinal fluid may be withdrawn with safety by means of lumbar puncture from any part of the intervening space. Lying between the posterior surface of the medulla and the cerebellum is a continuation upward of the posterior part of the spinal subarachnoid space. The cisterna pontis, in front of the medulla, is continuous with the anterior part

of the same space. The cisterna basalis stretches between the temporal poles and is in relation to the important interpeduncular space.

The subarachnoid space sends very important extensions filled with fluid into the substance of the brain. As the cerebral arteries pass into the brain they carry with them a fine, sleeve-like sheath which accompanies the vessel until it becomes a capillary. The wave of fluid resulting from a sudden blow may thus travel deep into the substance of the brain and give rise to those ecchymoses which have already been discussed in relation to concussion. The cerebrospinal fluid may therefore be compared to an expanse of water with rivers, innumerable rivulets, and a few deep lakes.

Absorption takes place into the great venous sinuses through the medium of the arachnoid villi, which are prolongations of the subarachnoid space projecting for the most part into the superior longitudinal sinus, and perhaps also directly from the subarachnoid space into the cerebral capillaries. The greater part of the absorption occurs above the level of the tentorium cerebelli, so that if some form of obstruction should prevent the flow of the fluid from the lower to the upper part of the cranial cavity hydrocephalus will result even although the aqueduct of Sylvius and the foramen of Magendie are both open.

The *pressure* of the cerebrospinal fluid, which is normally about 7 to 9 m.m. of mercury or 110 to 130 m.m. of normal saline, is always considerably above that of the sagittal sinus. Wegeforth demonstrated this in a striking manner by establishing an experimental communication between the subarachnoid space and the superior sagittal sinus. The opening in the wall of the sinus remained open for four days without hemorrhage occurring into the subarachnoid space. Lowering of the cerebrospinal fluid pressure by lumbar puncture, however, at once led to hemorrhage. The practical application of this observation to such a condition as subarachnoid hemorrhage in the new-born is obvious. Weed and McKibben, as already remarked, have recently shown that the pressure of the cerebrospinal fluid is markedly altered by the intravenous injection of solutions of various concentrations. Strongly hypertonic solutions lowered the cerebrospinal fluid pressure to an extreme degree whilst hypotonic solutions such as distilled water produced a prolonged rise. Cushing and Foley found that a similar effect could be produced by the ingestion of saline fluids.

Functions.—The function usually assigned to the fluid is a purely mechanical one, and no doubt it plays an important part in shielding the central nervous system from the rude shocks and blows of the outside world. The medulla, the most delicate and vital part of the brain, is surrounded by the cisterna magna and the cisterna pontis, so that the brain may be regarded as supported by a water cushion which serves to protect the more sensitive parts from harmful jarring.

Moreover, the fluid is able to flow from the cranial into the spinal cavity. As the skull is a rigid and inexpandable box this shifting of the fluid is of great value as a safety valve whereby the brain is permitted to expand. Even such acts as coughing or crying at once cause the fluid to flow out of the skull, and in cerebral congestion and edema and in the early stages of cerebral tumor this mechanism saves the brain from injurious pressure.

Important as these functions may be, there can be little doubt that the fluid is above all concerned with the nutrition of the central nervous system and the elimination of waste products. The cerebrospinal fluid bears a remarkable resemblance to Locke's physiological saline solution, which contains sodium chloride and a small quantity of glucose, and this is an ideal medium for nourishing the tissues and removing the products of metabolism. The cerebrospinal fluid, therefore, may be regarded as the lymph of the brain.

Diagnostic Value of Lumbar Puncture.—An examination of the cerebrospinal fluid affords valuable evidence, either positive or negative, in the following conditions: fracture of the skull, cerebral hemorrhage, meningitis whether acute, tuberculous, or syphilitic, cerebral abscess, cerebral tumor, and tumor of the spinal cord.

Fracture of the Skull.—If the fracture is accompanied by hemorrhage, and if the dura and arachnoid have been torn, blood will appear in the spinal fluid. This is most likely to occur in middle meningeal hemorrhage and in fractures of the base of the skull. Only positive evidence is of value. The absence of blood does not indicate the absence of a fracture.

Pathological blood must be distinguished from puncture blood. Collecting the fluid in two tubes, and centrifuging the fluid with examination for hemolysis, will usually settle the matter. If the hemorrhage is very recent there may be no hemolysis, as sufficient time has not elapsed for it to be produced. I have seen a case of fracture of the skull, examined within 24 hours of the injury, in which centrifuging removed every trace of blood. The source of the blood was evident, however, for it was so abundant and so constant in its flow that it could not possibly have come from the wounding of the plexus of veins which lies in the anterior wall of the spinal canal.

Cerebral Hemorrhage.—In cerebral hemorrhage, as a rule, no blood is found in the spinal fluid. It will appear there under two conditions: (1) if the hemorrhage bursts or even leaks into the ventricles, (2) if the surface of the brain is lacerated and the pia-arachnoid torn. Cushing has pointed out, moreover, that in the newly-born blood is often present in the spinal fluid owing to tearing of the delicate veins which pass from the cortex to the superior longitudinal sinus, the tear being produced by the strain induced by the moulding of the parietal bones.

Meningitis.—The diagnosis of meningitis depends upon spinal fluid examination. In acute meningitis the fluid is under pressure, turbid owing to the presence of pus, a coagulum forms which sticks to

the side of the tube, there is marked increase of the protein and an extremely high cell count, and the specific organisms can be found in smear or cultures.

In tuberculous and syphilitic meningitis the fluid is as a rule quite clear, although it may be slightly opalescent, there is a moderate increase in the protein, and a lymphocytosis of from 50 to 100; in the tuberculous variety a fine filmy clot forms, which floats like a cobweb in the center of the fluid, and in which tubercle bacilli can frequently be demonstrated if sufficient time be taken. In syphilitic meningitis the Wassermann reaction is usually but not invariably positive in the spinal fluid as well as in the blood.

Cerebral Abscess.—In abscess of the brain the condition of the spinal fluid should be helpful, but may be misleading. It will not mislead if it is borne in mind that a cerebral abscess may be associated with a perfectly normal fluid. Indeed it is the very negative character of the fluid which is of differential value in distinguishing abscess from meningitis, the condition with which it is most apt to be confused. If the abscess involves the surface, setting up a meningitis, or if it bursts into the ventricles, the fluid will be frankly purulent, and of much less differential value.

It may be advisable to perform more than one puncture, for changes in the cerebral pathology may be mirrored in the fluid which might otherwise pass unrecognized. Thus in a patient whom I saw some years ago, and who was suffering from severe headache and weakness of the left arm, the presence of a well-marked lymphocytosis in the spinal fluid suggested a return of a syphilitic affection which had produced headache and left hemiplegia two years before. A few days later the fluid became markedly purulent, and at the autopsy an abscess of the brain in the right motor area was found in addition to the remains of a syphilitic gumma which was evidently responsible for the lymphocytosis.

Cerebral Tumor.—The only reason why I have included cerebral tumor in the list of conditions in which lumbar puncture is of diagnostic value is in order to condemn the procedure. Lumbar puncture should never be done in a suspected case of cerebral tumor, except it be for the purpose of ruling out a syphilitic infection. The operation is not only dangerous but valueless. The high pressure under which the fluid spurts out is, it is true, an indication of a heightened intracranial pressure, but if the clinician is unable to diagnose such a heightening of pressure without laboratory assistance he would be well advised not to undertake the care of a brain case.

The danger is greatest in those cases where the tumor is situated in the posterior cranial fossa below the level of the tentorium cerebelli. The accident is usually due to the medulla being forced, as a result of the high pressure above and the lowered pressure beneath, like a plug into the foramen magnum with fatal pressure on the vital centers. To be more accurate, it is the amygdala of the cerebellum which is forced into the opening, and which in turn presses upon the medulla. The

groove produced by the pressure may be seen in fatal cases on the side of the cerebellar process. In a vascular sarcoma with thin-walled vessels a sudden fall in pressure may be followed by a fatal hemorrhage.

If the clinician is determined to do a lumbar puncture, not more than 2 c.c. of fluid should be withdrawn, and if the fluid spurts out the operator should at once pluck out the needle. Needless to say, the patient should be in the recumbent posture.

Tumor of the Spinal Cord.—If a tumor of the cord divides the spinal canal into two compartments, the lower of which is a cul-de-sac, the

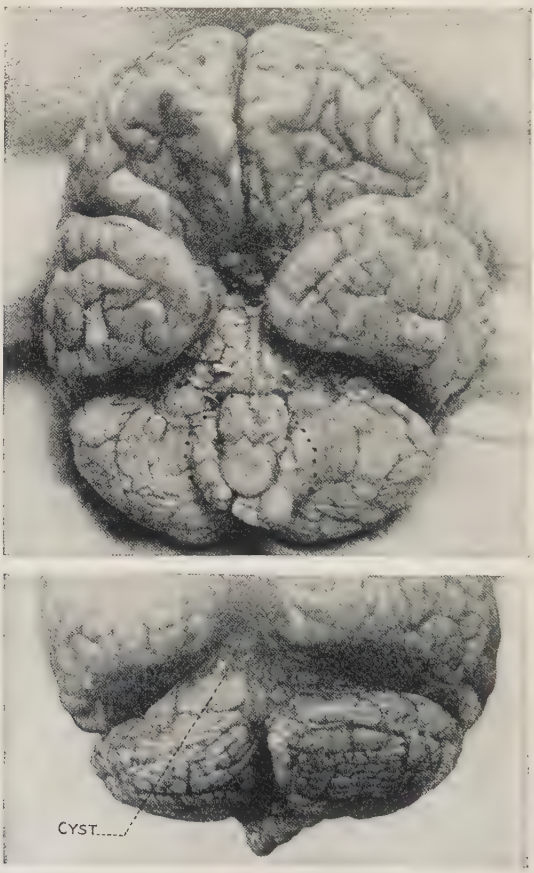


FIG. 255.—Brain of adult who died suddenly after withdrawal of fluid by lumbar puncture. Note cyst of left cerebellar lobe; also hernial mould of medulla and cerebellum crowded into foramen magnum, the imprint of the margin of which is shown by dotted lines. (Harvey Cushing in Keen's Surgery.)

spinal fluid will usually show the very characteristic change known as the *Nonne-Froin syndrome*. In its fully-fledged form this consists of the following: (1) yellow coloration of the spinal fluid (xanthochromia), (2) a great increase in the protein without any corresponding increase in the cell count, and (3) spontaneous coagulation. Of these

the second is much the most important, the third is seldom seen, and xanthochromia may occur in other conditions such as slight cerebral hemorrhage. The full syndrome, moreover, may be produced by any lesion, such as Pott's disease or a tumor of the spine, which will divide the canal into two segments. For a full discussion of the mechanism by which this peculiar condition is produced, reference must be made to monographs dealing with the cerebrospinal fluid.

HYDROCEPHALUS

Hydrocephalus was known to the ancients. But from the time when the father of medicine tapped the hydrocephalic ventricle down to the present day little has been added to our knowledge of the condition and practically nothing to its treatment, except that Magendie, Hilton, and others recognized the importance of obstruction to the exits of the cerebrospinal fluid in the roof of the fourth ventricle. During the last half dozen years, however, immense strides have been made both in the diagnosis and the treatment of the disease, and these advances have been almost entirely due to the work of Dandy and his associates at Johns Hopkins Hospital. The series of masterly papers in which Dandy has described his work should be consulted in full. Only a brief summary of his results can be given here.

The cerebrospinal fluid is produced in the ventricles and absorbed in the subarachnoid space covering the vertex of the brain. Anything which prevents the passage of the fluid from the place of production to the place of absorption will give rise to hydrocephalus.

The obstruction may occur at three points: (1) in the aqueduct of Sylvius, (2) at the foramina in the roof of the fourth ventricle, and (3) around the mesencephalon. The first two lead to *obstructive* hydrocephalus, the third to *communicating* hydrocephalus, so called because free communication exists between the ventricles and part at least of the subarachnoid space. The anatomical changes depend entirely on the site of obstruction.

In order to determine the type of hydrocephalus in any particular case Dandy has introduced three tests. (1) Phenolsulphonephthalein when injected into the normal ventricle appears in the spinal fluid obtained by lumbar puncture. This is also true for the communicating type of hydrocephalus, but not for the obstructive type. (2) When the spinal fluid is replaced at autopsy by Indian ink, the entire surface of the brain is stained with the pigment. In obstructive hydrocephalus the ink does not enter the ventricles, but reaches the surface of the cerebrum. In the communicating type the dye does not pass beyond the mid-brain. (3) In the living patient air is used instead of Indian ink, being injected either into the spinal sac or into the ventricles. An X-ray picture will then show clearly the outline of the ventricles and whether the air has reached the sulci on the surface of the cerebrum. By this method the exact site of the obstruction can be determined with the greatest accuracy.

The cerebrospinal fluid after escaping through the foramina of Magendie and Luschka enters the basal cisterns, and passes forwards to the pontine and mesencephalic cisterns, whence it ascends through the narrow opening in the tentorium cerebelli to the upper surface of the brain, where practically all the absorption takes place. It therefore follows that any obstruction in the narrow waters around the midbrain will be followed by a damming up of fluid, and a distension not only of the basal cisterns but also of the entire series of ventricles. All

FIG. 256.—Moderate degree of hydrocephalus.

forms of hydrocephalus are thus in reality obstructive, the differences depending on the site of the obstruction.

The experimental work of Dandy has proved this beyond dispute. By plugging the aqueduct of Sylvius he produced distension of the third and lateral ventricles. When the foramen of Munro on one side was blocked the corresponding lateral ventricle became dilated. If the choroid plexus was first removed before the foramen was plugged, the ventricle was found to be empty and collapsed, as the source of the

fluid had been destroyed. Blocking of the foramina in the roof of the fourth ventricle by means of an artificially produced local inflammation resulted in dilatation of all the ventricles. Adhesions were produced around the mid-brain by packing with gauze soaked in iodine, and the result was a typical communicating hydrocephalus with dilatation of basal cisterns, foramina of Magendie and Luschka, and the entire system of ventricles.

It is probable that meningitis is responsible for the adhesions which produce the vast majority of cases of communicating hydrocephalus due to occlusion of the foramina of Magendie and Luschka. In some instances a definite history of meningitis can be obtained, in others it is indefinite or absolutely lacking. The adhesions are not necessarily

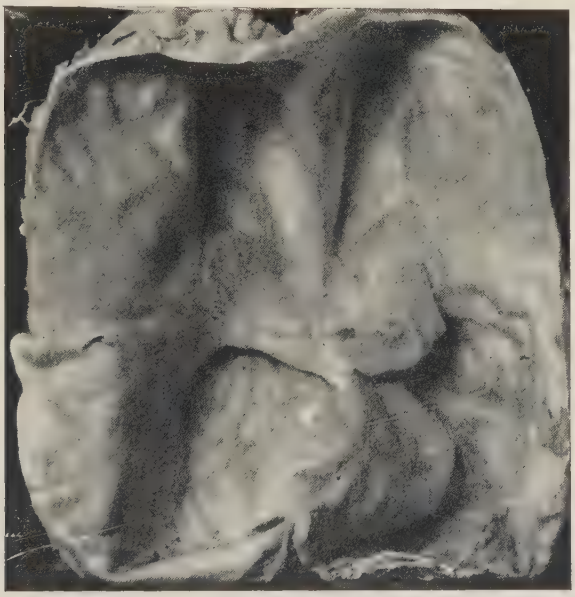


Fig. 257.—Hydrocephalus. The ventricles are enormously dilated, and the substance of the cerebrum is reduced to a mere shell. The brain stem and cerebellum, however, were practically normal, so that the vital centers in the medulla were not interfered with.

in proportion to the severity of the meningitis, and the occlusion depends rather upon the site than the number of the adhesions.

Stenosis of the aqueduct of Sylvius, although occasionally caused by the pressure of a tumor, is usually due to the formation of scar tissue. This is the principal cause of congenital hydrocephalus and a frequent cause of the cases occurring in infancy and early childhood. The stenosis may involve only a part or may occupy the whole of the canal. There may be only a thin veil of membrane across the lumen.

It is not possible to say with certainty what is the exact cause of this cicatricial tissue. Probably it is due to some slight intrauterine

inflammation destroying the epithelial lining of the canal. The aqueduct is the weakest link in the ventricular chain owing to its length and the narrowness of its lumen. A trivial lesion, which would pass unnoticed elsewhere, may therefore be attended by disastrous consequences in this region.

Whatever be the type of the disease, and in whatever way it may be caused, the appearance of the patient is characteristic. The cranium is fearfully enlarged, dome-shaped, and surmounts the little wizened face like an enormous turban. In the late stages the appearance is revolting, the head resembling a great quaking bag of jelly on which, here and there, can be felt the widely separated cranial bones. The cerebrum is thinned to a mere shell by the huge distension of the ventricles, but the cerebellum and the vital centers at the base may be wonderfully intact. The intelligence is always affected, often to an extreme degree, but the condition, although usually progressive and ultimately fatal, may allow the patient to drag out a vegetative existence for a number of years. The end may come from rupture externally or from excoriation of the skin with a resulting meningitis.

Fig. 258.—Hydrocephalus.

The elucidation of the pathology of hydrocephalus at least makes it possible to hope for success in the operative treatment. Dandy has already reported cases in which he has successfully established a permanent opening in place of the closed foramen of Magendie, and he has even been able to reestablish the patency of the aqueduct of Sylvius. Further discussion of the operative treatment would be out of place here.

MENINGOCELE AND ENCEPHALOCELE

These conditions are much rarer than the corresponding condition in the spine. A meningocele is a protrusion of the meninges through a congenital defect in the skull. The dura and arachnoid mater are involved, so that the sac is an extension of the subarachnoid space,

and is distended with cerebrospinal fluid. In an encephalocele the brain substance itself is extruded.

The two common sites are the occipital region and the frontal region close to the root of the nose; much rarer are the lower parietal region and the line of the sagittal suture; very rarely the protrusion is through the floor of the skull into the naso-pharynx where it may be mistaken for a polypus.

It is probable that there is a close causal connection between these conditions and hydrocephalus. The latter is often associated with cephaloceles, and the resulting pressure may well be responsible for a protrusion between the ununited bones of the infant skull.

Traumatic Cephalhydrocele.—In rare cases it happens that fracture of the skull in infancy is followed by the development of a cystic swelling at the seat of fracture. This is due not to a protrusion of the membranes, but to an actual escape of cerebrospinal fluid into the tissues, the result either of tearing of the arachnoid by the trauma, or laceration of the brain substance with opening up of the lateral ventricle. The swelling rapidly becomes larger, and the opening in the skull may increase in size to a remarkable degree owing to absorption of the bone.

TRAUMATIC INTRACRANIAL HEMORRHAGE

Intracranial hemorrhage due to injury may belong to one of the following groups:

1. Extradural hemorrhage,
2. Subdural hemorrhage,
3. Subarachnoid hemorrhage,
4. Intracerebral hemorrhage.

1. **Extradural Hemorrhage.**—This is essentially arterial meningeal hemorrhage due to fracture of the skull. In the vast majority of cases it is the middle meningeal artery which is involved, usually at the anterior inferior angle of the parietal bone, but occasionally when traversing the squamous portion of the temporal. The elastic recoil of the skull under the blow produces an initial separation of the dura from the bone, a separation which gradually increases as blood is poured out. After a *lucid interval* of a few hours symptoms of compression appear, and there may be evidence of pressure on the motor area. There is, of course, no blood in the cerebrospinal fluid. Unless treated promptly the condition usually proves rapidly fatal. At operation or autopsy a large clot is found between the dura and the bone, and there may be great flattening or even indentation of the brain. Should recovery take place it is rare to have any cyst formation.

2. **Subdural Hemorrhage.**—Hemorrhage into the subdural space is perhaps the commonest variety of traumatic hemorrhage. It may come from (1) large arteries, such as the internal carotid or the middle

cerebral, (2) the large venous sinuses, particularly the superior longitudinal, the lateral, and the cavernous sinuses, and (3) the cerebral veins passing from the cortex into the sinuses. As the first variety is rapidly fatal and of no surgical interest, it is evident that for practical purposes subdural hemorrhage may be regarded as venous in character, just as extradural hemorrhage is arterial. Its progress, therefore, will be slower, and it will be less likely to prove fatal.

The hemorrhage may be *diffuse*, covering the greater part of one hemisphere, or, owing to rapid clotting of the blood, it may remain *localized* to one part of the subdural space, and may there give rise to definite localizing symptoms demanding operation. The blood seldom succeeds in spreading from one side of the brain to the other unless the injury be at the base. Bilateral hemorrhage, however, is quite frequent owing to the injury produced on the other side at the point of contre-coup.

If the arachnoid is torn, as it is apt to be over the great cisterns at the base, the blood will escape into the subarachnoid space and will be found in the cerebrospinal fluid.

The subsequent changes which the clot may undergo are of importance. If death does not supervene, a limited amount of the blood may be absorbed, but the greater part becomes encysted. The clot becomes softened and liquefied so as to form a cyst, the walls of which consist at first of fibrin but later of a very tough fibrous membrane. The contents are brown or greenish, but in course of time the blood pigment is absorbed, and masses of cholesterin crystals take its place. The cyst can be stripped from the brain on the one side and from the dura on the other. It sometimes happens that after a long period such a cyst will begin to enlarge for no known reason, and may give rise to symptoms suggestive of cerebral tumor.

Intracranial Hemorrhage in the Newborn.—The cerebral veins passing from the cerebral cortex across the subdural space into the superior longitudinal sinus are injured more frequently at birth than is generally supposed. There is no fracture of the skull, the trauma being due to the moulding of the head or the use of instruments, with as a subsidiary factor the strain thrown on the vessels by asphyxia or by efforts at artificial respiration. At autopsy in fatal cases tears are frequently found in the tentorium cerebelli or the falx cerebri. These lesions are easily overlooked unless special precautions are taken in the performance of the autopsy. The condition is most frequently met with in premature children and in breech presentations.

The blood is poured into the subdural space, but the arachnoid is frequently torn, so that blood is found in the cerebrospinal fluid. Lumbar puncture, therefore, is a valuable means of diagnosis. As the extravasation is most marked over the upper portion of the cerebral surface the leg centers are the ones to suffer most. A degree of hemorrhage which in an adult would certainly prove fatal can be compensated in the child by the elasticity of the skull and the safety valve action of the fontanelle.

Two types of cases may be distinguished. In the first the injury is sufficient to cause serious hemorrhage in an otherwise normal child. In the second the damage may be so slight that under ordinary circumstances it would not amount to anything, but, owing to a hemorrhagic diathesis—a condition in which there is a great increase in the coagulation time and bleeding time—the hemorrhage does not stop. These cases can readily be recognized by a simple test of the coagulation time of the blood, and they can be treated very successfully by subcutaneous injections of whole blood.

Amongst the more immediate symptoms are a tendency to asphyxia, slow pulse, irregular respiration, twitching movements, and a bulging anterior fontanelle. Later paralytic symptoms appear, the most common of which is the spastic paraplegia known as Little's disease. The motor area may not be involved, but serious mental defects, epilepsy, and other disastrous sequelæ may take the place of the motor symptoms.

If the condition is diagnosed early and the blood clot localized brilliant results may be obtained by clearing out the contents of the subdural space.

3. **Subarachnoid Hemorrhage.**—Hemorrhage into the subarachnoid space is usually the result of laceration of the brain, but it may complicate a subdural hemorrhage if the arachnoid be torn. When the hemorrhage is into the large open cisterns at the base of the brain death soon results from pressure on the medulla. Over the cortex, on the other hand, the subarachnoid space is greatly subdivided by the numerous septa which traverse it, so that the blood infiltrates the network rather than forms a large and massive clot. For this reason operative treatment is much less satisfactory than in subdural hemorrhage. In this variety blood is always present in the cerebrospinal fluid.

4. **Intracerebral Hemorrhage.**—This variety of hemorrhage may be due to spontaneous rupture of an artery in the interior of the brain, a condition of interest to the physician rather than to the surgeon. Or it may be traumatic in origin.

Traumatic hemorrhages, occurring as they frequently do as a complication or accompaniment of concussion, have already been alluded to. They are of two varieties.

1. Numerous small petechial hemorrhages, scattered throughout the brain, although usually most marked in one region, and due probably to the cerebrospinal wave which results from the trauma.

2. Larger hemorrhages the result of the laceration of the brain, and principally affecting the surface, although often extending for some distance into the interior. Such a hemorrhage consists of (1) a central clot, (2) a zone of liquefying brain substance of a red color, and (3) an area dotted with minute hemorrhagic points. Ultimate cyst formation is very common, as in so many brain lesions. The hemorrhage may be most marked at the point of contre-coup on the opposite side of the head from the seat of the trauma.

A somewhat rare occurrence is the onset of symptoms of cerebral hemorrhage some days after the receipt of an injury to the head. This is supposed to be due to a focus of cerebral softening implicating a vessel and thus giving rise to a secondary hemorrhage.

It frequently happens that in a patient with a history of having fallen heavily on the head a large hemorrhage is found in the basal ganglia. This is a spontaneous hemorrhage from one of the branches of the middle cerebral artery, and the fall was the result and not the cause of the hemorrhage.

INTRACRANIAL SUPPURATION

Suppuration within the cranial cavity may take one of four chief forms: (1) extradural abscess, (2) meningitis, (3) cerebral abscess, and (4) sinus phlebitis.

Extradural Abscess.—Infection may spread inward from the skull and give rise to local suppuration between the bone and the dura mater.

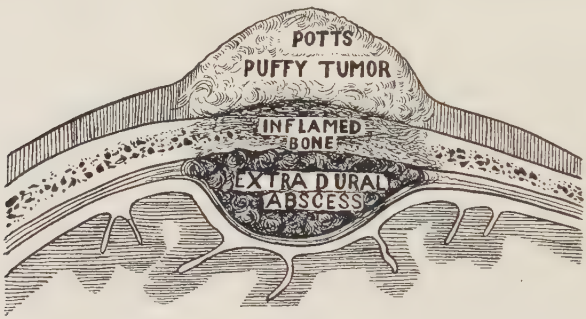


Fig. 259.—Pott's puffy tumor in extradural abscess.

The primary seat of the infection is usually an osteomyelitis of the cranium, middle ear or frontal sinus disease, or a compound fracture of the skull.

A localized collection of pus is formed external to the dura, and as the dura is remarkably impervious to infection it may be a considerable time before a general meningitis or a cerebral abscess complicates the picture. An interesting feature of the disease is the development of the condition described in so masterly a manner by Percival Pott in 1760 that it is still known as *Pott's puffy tumor*. The scalp over the abscess becomes swollen, puffy and edematous in just the same way as does the skin overlying an osteomyelitis. If a wound of the scalp is present the inflammatory material is able to escape, and the puffy tumor as a rule does not form.

In the frequent cases in which a subdural abscess complicates middle ear disease the inflammation is often of a somewhat chronic nature, and characterized by the formation of abundant granulations with comparatively little pus. These granulations may give rise to extensive rarefaction of the bone.

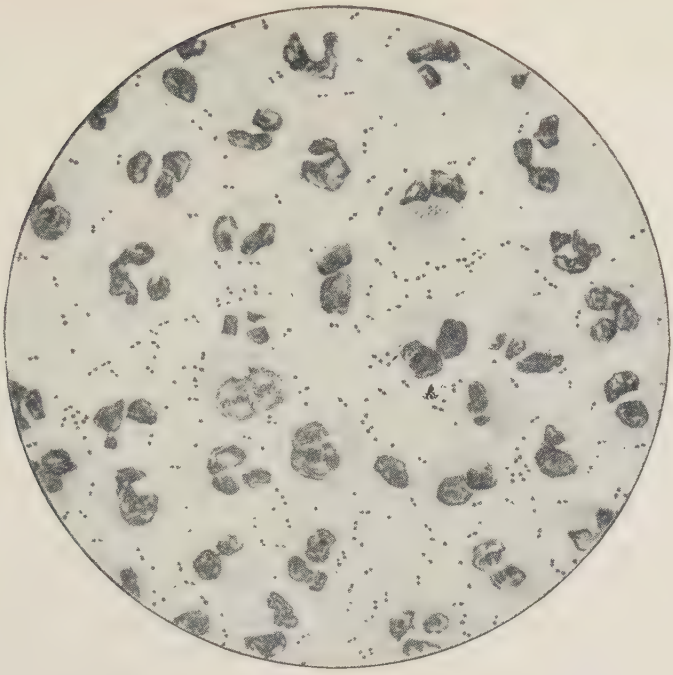


FIG. 260. –Cerebrospinal fluid in pneumococcal meningitis.

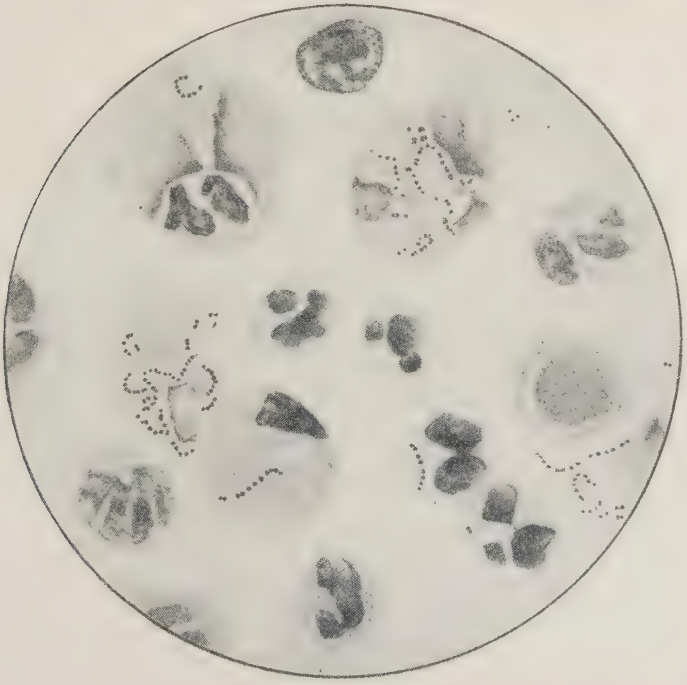


FIG. 261.—Cerebrospinal fluid in streptococcal meningitis.

Acute Meningitis.—This is hardly the place in which to discuss the different varieties of meningitis, but it may be said that the organisms found in order of frequency are the meningococcus, the pneumococcus, and the streptococcus. Infection usually spreads from some neighboring focus such as the nasopharynx, the middle ear, the frontal sinus, a compound fracture of the skull, a patch of osteomyelitis, a subdural abscess, or a cerebral abscess. Meningitis may, in short, complicate any form of intracranial suppuration.

The final diagnosis is made by means of lumbar puncture. The cerebrospinal fluid under pressure, and of varying degrees of turbidity, shows a great increase of protein, and is crowded with pus cells. In the pneumococcal and streptococcal forms the organisms can usually be found in large numbers in the direct smears. In the acute cerebrospinal meningitis due to the meningococcus it is sometimes impossible to find any diplococci in the smears, and culture must be resorted to.

Abscess of the Brain.—A cerebral abscess is never primary, but always secondary to some other focus of infection. The primary causes may be grouped in their order of frequency as follows:

1. Suppuration of the middle ear, and, much less frequently, of the frontal and nasal sinuses.

2. Trauma, whereby infection is carried into the interior of the brain either by a missile, or as the result of a compound fracture of the skull.

3. Pyemia, the infection being carried from some distant source of infection. Of particular interest is the frequency with which septic pulmonary conditions, especially bronchiectasis and more rarely empyema, are complicated by cerebral abscess, a relationship which has never been explained.

4. Disease of the bones of the skull, such as osteomyelitis or syphilitic necrosis.

Of these causes by far the most important is middle ear disease. The infection does not pass in through the internal auditory meatus, but either upward through the tegmen tympani, or along the veins into the substance of the brain. In the former case the path of infection can be readily traced, for the bone is eroded and there is a mass of granulation tissue between the dura and the bone, or it may be a definite subdural abscess. It is remarkable how often there is no general meningitis; although the infection must traverse the subarachnoid space, the adhesions which form are sufficient to prevent a general spread.

When the infection spreads by the veins, or it may be by the lymphatics, the surface both of the bone and of the brain may appear perfectly healthy.

The lower part of the temporo-sphenoidal lobe is the seat of election in the middle ear cases, although the cerebellum is affected in a certain number of cases. An abscess in the former situation may remain "silent" as regards localizing signs, or it may give rise to

paralysis. If the abscess extends upwards first the face, then the arm, and finally the leg may be affected, owing to the gradual involvement of the cortical centers which are arranged in that order. If it extends inwards first the leg, then the arm, and finally the face are involved, since the fibers in the internal capsule are arranged in that order from behind forward.

A cerebral abscess is usually single, but may be multiple, especially when due to pyemia. In the acute stage the surrounding brain tissue is inflamed, soft, infiltrated with pus. Later, if the patient does not

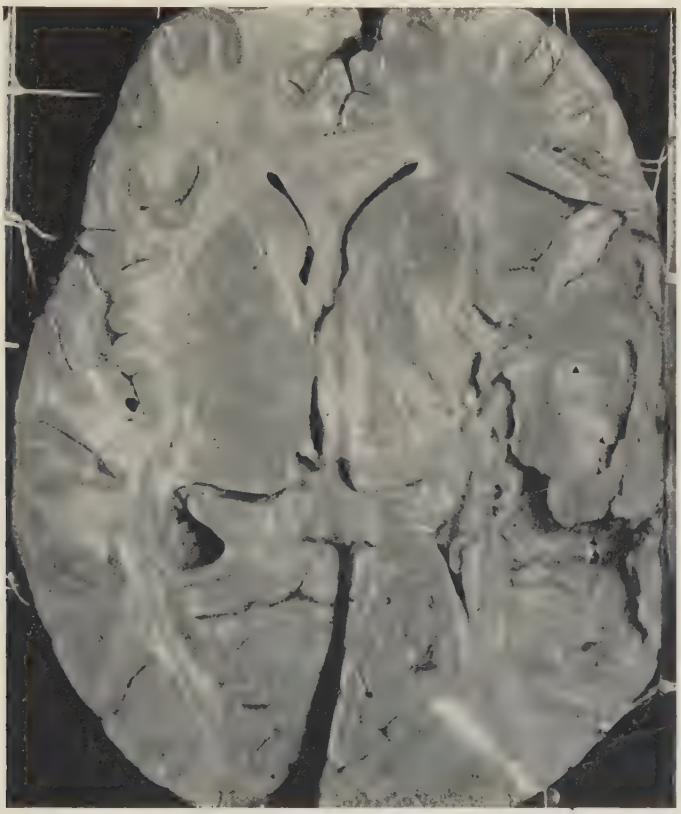


Fig. 262.—Temporo-sphenoidal abscess secondary to middle ear disease.

die, a well-marked capsule of condensed tissue may form around it which effectually prevents either spread or absorption of the toxic products. It is usually six weeks before such a capsule is produced.

The contents of the abscess are greenish in color, perhaps tinged brown with blood, and often of an offensive odor. Staphylococci, streptococci, and pneumococci are perhaps the organisms most frequently found, but many other varieties may be present, amongst which may be mentioned B. pyocyaneus.

The cerebrospinal fluid is unaltered, apart from increased pressure and a trace of globulin, a point of great value in differentiating abscess from meningitis. In abscess, moreover, there are not the same signs of septic absorption as are found in meningitis, the temperature may be normal or subnormal, the pulse is abnormally slow, and the leucocytosis in the blood is moderate compared with the hyperleucocytosis of meningitis.

The chronicity of some brain abscesses is remarkable. A localized collection may remain in the brain for many months producing wonderfully little disturbance. Eventually, however, it will almost always

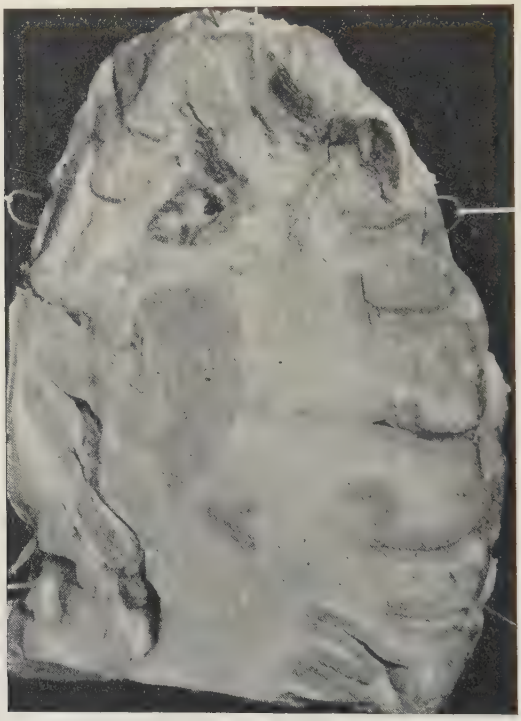


Fig. 263.—Chronic abscess of brain due to shrapnel wound. Perforation into lateral ventricle can be seen.

rupture into the ventricles or on to the surface, where it produces an acute and fatal meningitis. During the war the presence of a foreign body in the brain not infrequently gave rise to a cerebral abscess quite a long time after the initial injury. In the University of Manitoba Pathological Museum there is a brain showing a tiny abscess of the frontal lobe which had ruptured into the lateral ventricle. Leading from the abscess to the surface a long scar marking the track of the original missile stands out prominently. Two years elapsed between the time the man was wounded and the date of his death due to the abscess

bursting into the ventricles, and during that period he only suffered from frontal headaches, dizziness on stooping, and a rare convulsive seizure, so that the presence of an abscess was entirely unsuspected.

Sinus Phlebitis.—The dura mater lining the skull consists of two layers which separate in places to enclose the cranial venous sinuses. These may become inflamed and thrombosed owing to the spread of infection from some neighboring focus. It is the same story that has already been repeated several times, and which need not be recapitulated in detail once more.

In brief, by far the commonest cause is inflammation of the middle ear, which spreads to the *lateral sinus.* The *superior longitudinal sinus* is infected from erysipelas and other septic conditions of the scalp, or from a compound fracture of the skull. Infection may reach the *cavernous sinus* from suppurative conditions in the face, nose, orbit, and sphenoidal air cells. Carbuncle of the face is regarded as a

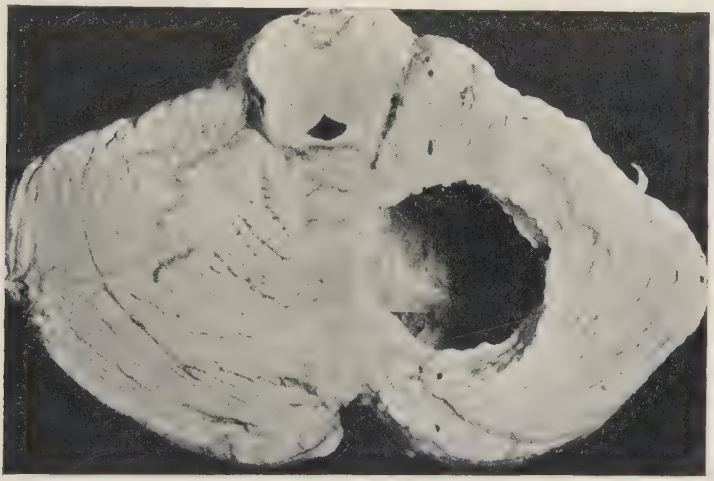


Fig. 264.—Cyst of cerebellum.

special black sheep in this respect. Cavernous sinus thrombosis is often bilateral, the infection passing to the other side by way of the circular sinus.

When infection reaches such a vessel as the lateral sinus, the endothelial lining becomes inflamed and roughened, and thrombosis occurs so that the vessel feels solid. The thrombosis being a septic one softening and liquefaction soon occur, and there is thus a tendency for septic particles to be carried off in the blood stream first to the lungs, where they set up numerous septic infarcts, characterized by sudden attacks of pleuritic pain and perhaps coughing of blood, and later throughout the body.

The thrombosis tends to spread down the internal jugular vein as well as to the other sinuses, and the vein may be felt as a hard and tender cord in the neck. This tendency for the thrombosis to spread,

although disastrous in some ways is yet beneficial in others, for the thrombotic process which occludes the vessel usually succeeds in keeping ahead of the liquefaction process which renders the clot so dangerous, so that there may be a considerable area of liquefied clot in the vessel, a veritable abscess, which is nevertheless securely shut off from the general circulation. The sword of Damocles, however, is suspended by a very thin thread, and disaster may overtake the patient at any moment.

The infection may spread outward, if it has not already come from that direction, and give rise to a fatal general meningitis, or in some cases a cerebral abscess. Or, as already mentioned, it may spread downward into the jugular vein or forward into the other sinuses. In a recent autopsy the lateral, petrosal, and cavernous sinuses on both sides were filled with a septic semi-liquid clot, the infection having crossed to the other side via the circular sinus. The jugular vein had been ligatured, so that no downward spread was possible.

The *clinical picture* of sinus thrombosis is very different from that of cerebral abscess. The course of the former is stormy and tempestuous compared with the comparative calm and peace of the latter. The relation to the blood stream is, of course, amply sufficient to explain the difference in the two cases.

TUMORS OF THE BRAIN

The subject of cerebral tumors is so intricate and complicated that it cannot be discussed here with any degree of fullness. The current views regarding the pathological nature of these neoplasms will be found in a paper by Greenfield in Brain, 1919, vol 42, part 1. The subject has acquired fresh surgical interest from the recent work of Dandy both on the localization of cerebral growths by means of cerebral pneumography and on the thorough and radical removal of these growths. Just as the urologist can localize the lesions in the kidney and the ureter by filling the urinary channels with a substance opaque to the X-ray, so the neurologist can fill the ventricle and the subarachnoid space with air and determine the presence of a tumor from the distortion of one or other of these cavities which it produces—a procedure, however, fraught with very great danger in any but expert hands.

The term cerebral tumor differs considerably as to whether it is used in a clinical or a pathological sense. The clinician means by it any solid mass of new tissue which may occur in the interior of the cranium, so that he includes tuberculoma and gumma in this group. The pathologist confines the term to true neoplasms. For purposes of convenience the clinical usage will be followed here.

Relation to Trauma.—In every part of the body one finds tumors the onset of which is imputed to a blow received at some recent or distant date. In most of these cases one is forced to the conclusion that it is merely one more example of the old fallacy *post hoc ergo propter*

hoc. In the brain, however, the evidence is sometimes more convincing and not lightly to be disregarded.

A recent case which came under my notice is particulary suggestive. The patient, a man of middle age, was in a run-away rig seven years ago. He was thrown out, fell on the back of his head, and remained unconscious for several days. On gradually regaining consciousness he was found to be suffering from a left-sided hemiplegia, and to be remarkably dull and stupid. The hemiplegia cleared up after a long interval, but he never regained his mental brightness. Six years later he began to suffer from headaches, the dullness deepened into something approaching his condition shortly after the accident, and, most remarkable of all, a slowly developing left-sided hemiplegia again made its appearance. In the course of time he died, and the autopsy revealed a very vascular large round-celled sarcoma behind the internal capsule on the right side and interrupting the optic radiation. The similarity of the symptoms produced by the initial trauma and by the subsequent tumor, taken in conjunction with the intervening mental condition which first cleared somewhat, then remained stationary, and finally deepened, points irresistibly to the conclusion that the trauma produced laceration and hemorrhage followed by scar tissue formation, which eventually served as a basis for the development of a sarcoma.

Secondary Effects.—A cerebral tumor produces secondary effects on the brain tissue, on the circulation of blood and cerebrospinal fluid, and on the skull.

The *brain tissue* in the neighborhood of the tumor shows atrophy from pressure. The irritation of the tumor may lead to a condition of edema not only in the immediate neighborhood but sometimes involving an entire cerebral hemisphere, thus accounting for the general enlargement of a hemisphere which is frequently observed even when the tumor is comparatively small. The most important complication of cerebral tumor is the increased intracranial pressure, and much of this increase may be due to edema. In fracture of the skull cerebral edema occupies a similar position of commanding importance; it is the edema rather than the fracture which eventually proves fatal. Secondary hemorrhage into a soft glioma or sarcoma is of frequent occurrence, and may be precipitated by the rash withdrawal of too large an amount of cerebrospinal fluid by lumbar puncture. The symptoms produced are those of apoplexy.

The operation of decompression has as its object the relief of intracranial pressure by the production of a cerebral hernia. The brain is allowed to protrude under the temporal muscle or the occipital muscles. But this protrusion does not necessarily mean a relief of intracranial pressure. If the pressure is due, as is so often the case, to an obstructive hydrocephalus, a decompression is worse than useless. As Dandy remarks, if surgeons would picture at operation the brain under a decompression several months after the operation, they would hesitate about performing the operation so casually. The temporal and occipital muscles must by their contractions continually irritate the protrud-

ing portion of the brain, so that adhesions form between the brain and the overlying muscles, fluid collects between the adhesions, the vessels are injured, and the brain undergoes softening.

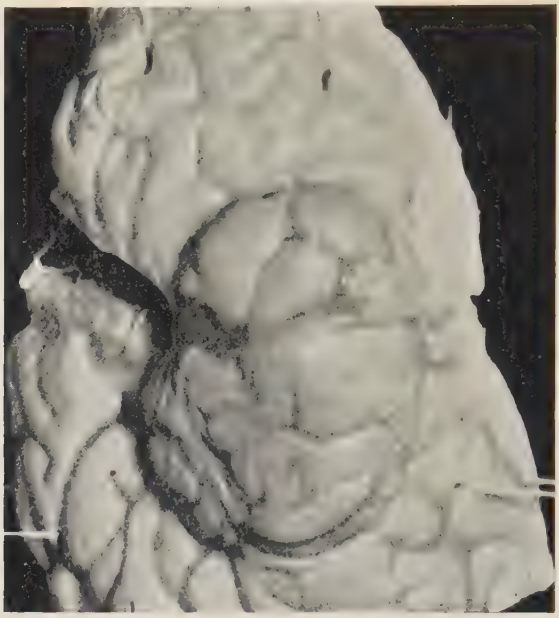


FIG. 265.—Effect on the brain of a decompression operation.

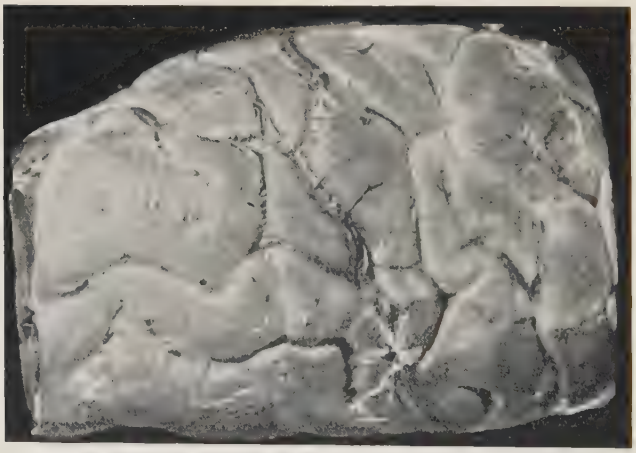


FIG. 266.—Flattening of the convolutions in a case of cerebral tumor.

The *circulation* of the brain must inevitably be interfered with. When examined at operation the convolutions are flattened, and none of the normal pulsation can be seen. The possibility of hydrocephalus

must always be considered. If a symmetrical hydrocephalus can be demonstrated by means of cerebral pneumography, the tumor must obstruct a channel between the aqueduct of Sylvius and the foramen of Magendie. In such a case, of course, there would be no object in performing an exploratory craniotomy. The subarachnoid space communicates normally with the lymph spaces in the sheath of the optic nerve, and the effect of fluid being forced into these spaces under high pressure is to obstruct the venous return along the nerve although still leaving the artery open, with the resulting edema and hemorrhage characteristic of choked disc.

The *skull* may be thinned in places from pressure, although as a rule this is seen in children rather than in adults. Tumors of the base, however, may produce marked destruction. I have studied a case of pituitary tumor in which the floor of the sella turcica was occupied by a yawning cavity communicating with the nose. When the patient sat up in bed a clear watery fluid used to drop from his left nostril, an example of cerebrospinal rhinorrhea.

The principal intracranial tumors are glioma, sarcoma, and endothelioma or meningioma, to which may be added tuberculoma and gumma, although these are not true neoplasms.

Glioma.—The most frequent and characteristic tumor of the nervous system is the glioma, found not only in the brain but also in the spinal cord. Although commoner in early adult life it may also occur in later years. When the skull is opened no trace of a tumor may be seen, and even when the brain is incised it may not be easy to distinguish the growth from the brain substance. A greyish gelatinous tumor, infiltrating the brain substance but causing little alteration in its appearance, is almost certainly a glioma. Usually it is either a little softer or a little firmer than the surrounding brain, greyish-white in color, and splashed with opaque yellow areas of necrosis or red areas of hemorrhage. There may be cyst formation as the result of the softening.

The tumor may be occupied by a large hemorrhage, which may lead to a wrong diagnosis of apoplexy. In every case of cerebral hemorrhage it is well to keep two possibilities in mind: (1) that the condition may be one of tumor complicated by hemorrhage; (2) that it may be a case of epidemic encephalitis.

The *microscopic structure* of a glioma varies considerably. The glia fibers are the most characteristic feature; they can be stained differentially with Mallory's phosphotungstic acid-hematoxylin provided that the material is quite fresh. The glia cells may take various forms. Often they are rounded cells with a darkly staining nucleus, closely resembling sarcoma cells. Or the cells may be typical astrocytes or spider cells with numerous branched processes. Occasionally large multinucleated cells predominate and to these the name of giant-cell glioma has been given. Such tumors, whose cells resemble ganglion cells, are found particularly in the neighborhood of the ventricles, and it has been suggested that they represent a harking back to the original

neuro-epithelial cells from which both the ganglion cells and the glia cells are derived. In one such case which I studied the tumor, which arose from the septum lucidum and was situated in the center of the third ventricle, contained so many of these large cells as to resemble a giant-cell tumor of bone. A tail-like process of the growth projected into the commencement of the aqueduct of Sylvius and produced an extreme degree of hydrocephalus. In rare instances the cells of a glioma may surround a lumen, again suggesting an origin from the cells of the neural canal.

Retinal Glioma.—Reference may be made here to the interesting tumor known as glioma of the retina. It presents three striking clinical characteristics: (1) it is bilateral in over 20 per cent of the cases; (2) two-thirds of the cases occur before the fourth year; (3) it displays a

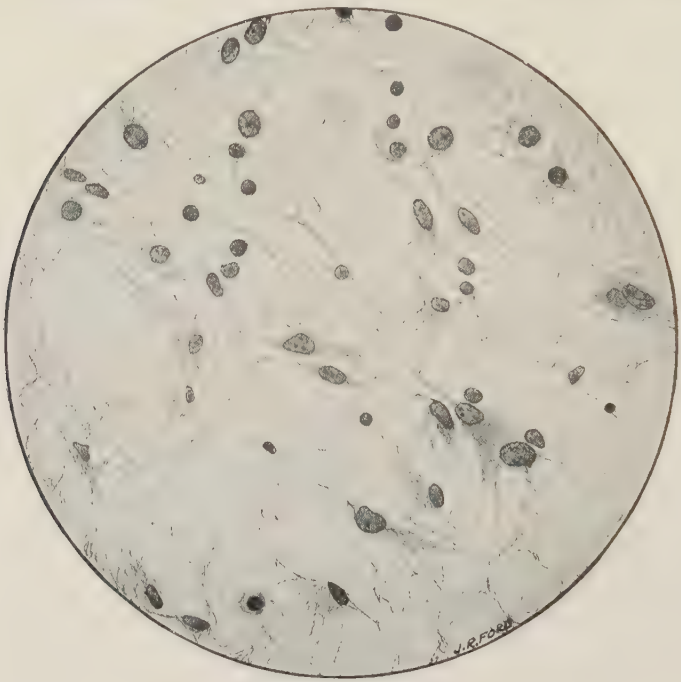


Fig. 267.—Glioma: glial cells and fibers.

most remarkable familial tendency. Newton reports a family of 16 children of whom 10 died of glioma of the retina, 7 of the cases being bilateral. The exact nature of this tumor is still a matter of debate. Although by many it is held to be a glioma, it is equally probable that it should be regarded as a neurocytoma or neuroblastoma of the same nature as the tumors of nervous origin which arise in the anlage of the sympathetic system, more particularly in the adrenal medulla. The same rosette-like clumping of the cells around little bundles of neurofibrils may be seen; in some cases there is a perivascular mant-

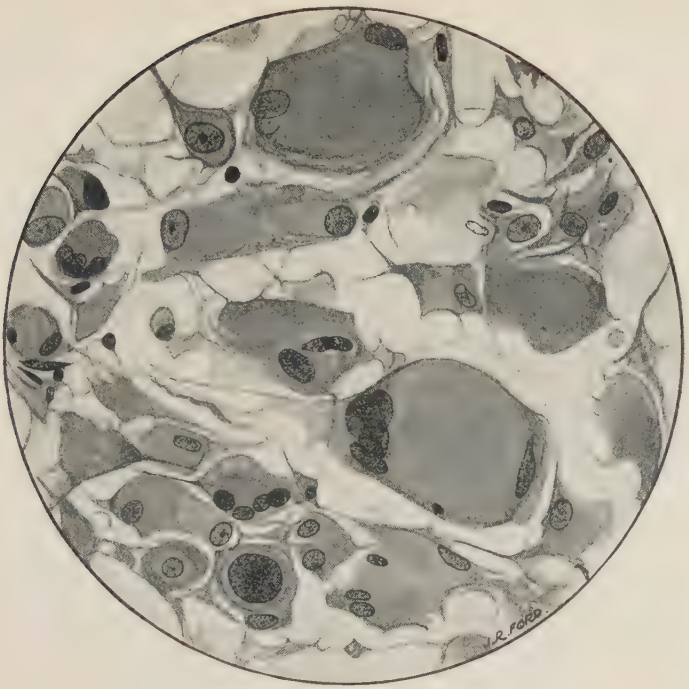


FIG. 268.—Giant-cell glioma.

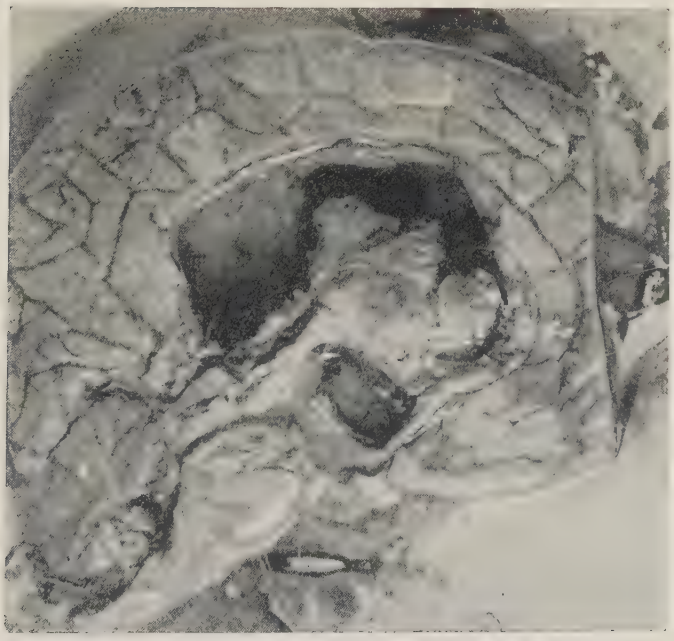


FIG. 269.—Tumor of the septum lucidum. The tail-like process of the tumor blocked the entrance of the aqueduct of Sylvius and caused a marked degree of hydrocephalus.

ling of living cells, those farther away from the vessel dying and failing to take up the nuclear stain.

Sarcoma.—Sarcoma of the brain is probably a much rarer disease than used to be thought, the majority of the supposed cases proving

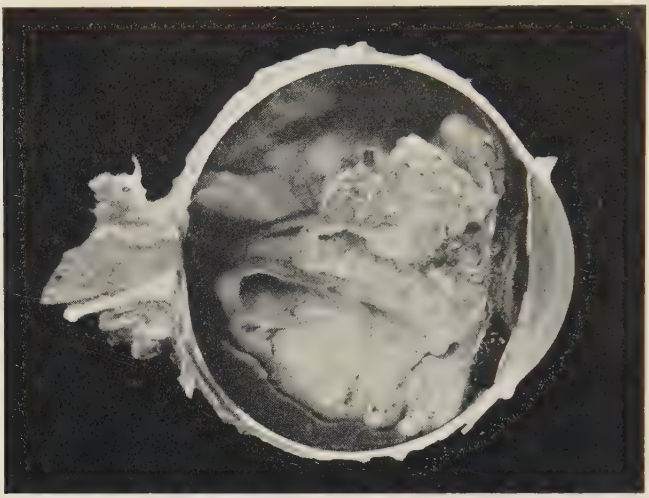


FIG. 270.—Glioma of retina. (Ewing.)

on further examination to be gliomata. A sarcoma, being a tumor of connective tissue origin, must arise either from the meninges or from the walls of the blood vessels within the brain. Although usually

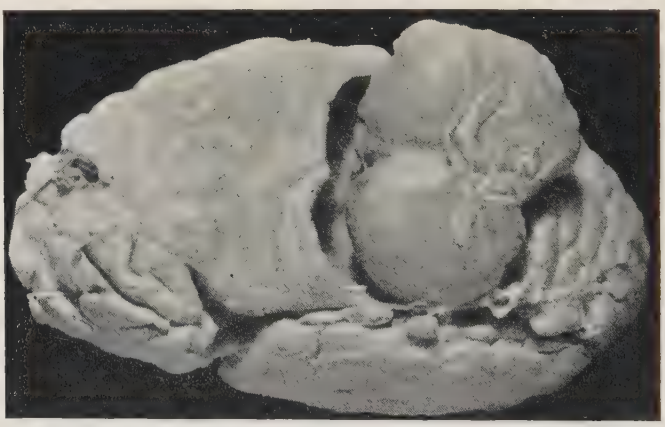


FIG. 271.—Meningeal endothelioma. The encapsulated nature of the tumor and the depression in the brain are well shown.

originating in the membranes it invades the brain extensively, and is often distinguished with difficulty from a glioma. A sarcoma invades the skull in a way that the glioma never does.

Meningioma.—A large number of names have been applied at various times to this tumor, the most commonly employed being that of dural endothelioma. The term psammoma, originally introduced by Virchow, is undesirable because it merely indicates a special form of degeneration which may occasionally occur, associated with the deposition of lime salts. In a recent lecture Harvey Cushing has suggested the non-commital term meningioma, which in many ways is preferable to any of those in use. In Cushing's large series of cases there was one meningioma to every four gliomas.

The condition is not a true tumor of the brain, for it does not originate from the brain. Nor does it arise from the dura mater, as its

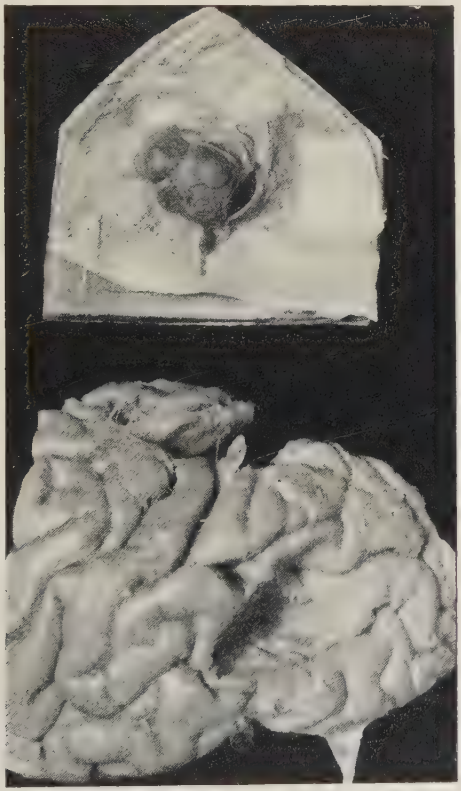
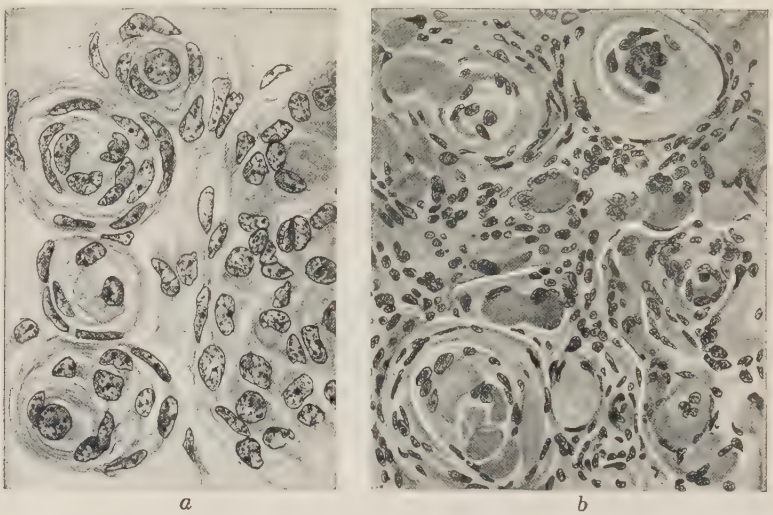


Fig. 272.—Meningeal endothelioma showing effects of pressure on the brain.

common name suggests. Its site of origin is the arachnoid mater, in those groups of mesothelial cells which are found in connection with or close to the arachnoid villi. Meningiomas are found in the spinal canal where they take origin from the arachnoid at the point of emergence of one of the nerve roots; at the foramina of exit of the cranial nerves, particularly the second, fifth, and eighth; above the sella

turcica; over the convexity of the brain. The last named is perhaps the most common site.

The tumor may grow into the brain to such an extent that it may appear to be completely surrounded by cerebral substance and show no connection with the arachnoid, but it is usually well encapsulated, so that it can be readily shelled out. Microscopically it consists of masses of endothelial cells which may show a whorled arrangement. Psammoma bodies may be present; they are hyaline spherical bodies showing concentric lamination, and are similar to corpora amylacea, except that they contain lime salts. If favorably situated and correctly diagnosed, no tumor is more amenable to surgical treatment. The tumor depicted in Fig. 272 produced hemiplegia of a year's standing, the patient eventually dying of acute appendicitis.



a *b*

FIG. 273.—Dural endothelioma. *a*. Whorls of endothelial cells and fibroblasts; *b*, whorls of endothelial cells around (necrotic) hyaline masses of collagen fibrils. (Mallory.)

One of the most interesting features of the meningeal endotheliomas is the occurrence of *local changes in the skull* overlying the tumor. These changes may be of two types—local erosion or local bony thickening. Erosion, with, it may be, perforation of the skull, is of rare occurrence. Local bony thickening is much more common. Cushing found cranial hyperostosis in 25 per cent of 80 cases of meningeal endothelioma. The hyperostosis is due to penetration of the dura and direct invasion of the skull by the tumor. Phemister has shown that the new bone is not tumorous in nature, but merely the ossified stroma of the invading endothelioma which permeates both the inner and the outer tables of the skull.

Acoustic Nerve Tumors.—A tumor quite distinct from those already considered is that which occurs in the cerebello-pontine angle.

It forms a firm, round, lobulated swelling, as a rule is well encapsulated, and lies quite outside the brain. It is of the same nature as the multiple neurofibromata of von Recklinghausen's disease, and may be associated with the presence of multiple peripheral tumors. In his

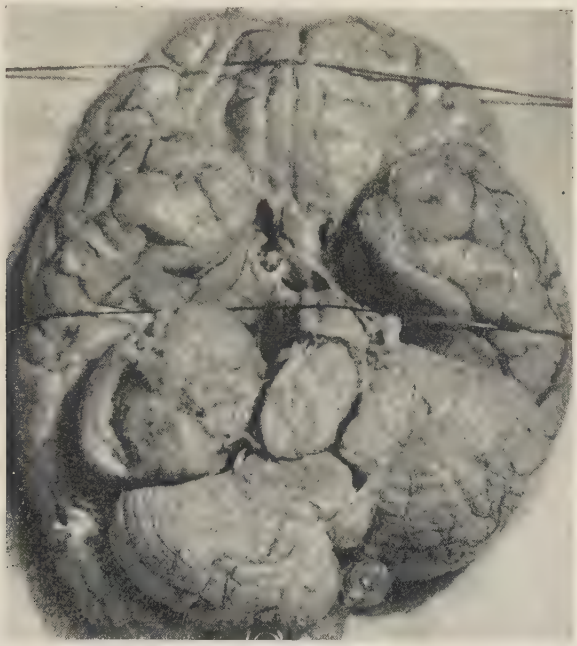


FIG. 274.—Tumor of the nervus acousticus (cerebello-pontine angle tumor). Marked displacement of the pons and cerebellum.

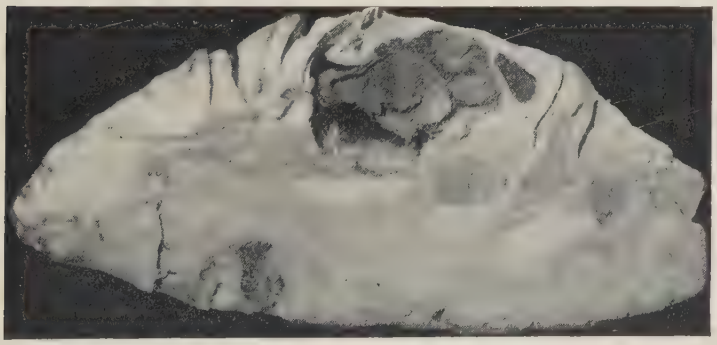


FIG. 275.—Secondary melanotic sarcoma in brain. Several large masses are scattered throughout the cerebral hemisphere.

recent monograph Harvey Cushing has shown that the tumor is usually situated within the internal auditory meatus which is markedly enlarged. He considers that it arises from undifferentiated cells at the

junction of the glial elements with the sheath of Schwann, and that it is essentially a tumor of the sheath of Schwann.

Diffuse Sarcomatosis of the Meninges.—Although tumors of the central nervous system are usually circumscribed and tumor-like in appearance they may occasionally lose their tumor character and take on the form of a diffuse meningeal process to which the name of diffuse sarcomatosis has been given. This peculiarity, however, is by no means confined to sarcoma, for it may be manifested by glioma, secondary carcinoma, primary or secondary melanoma, and angioma. The malignant cells infiltrate the pia mater, forming a mantle over but rarely invading the brain. Frequently the meninges of both the brain and spinal cord are involved, but the disease may be confined to one or other of these organs. Small secondary growths may be studded over the ependyma of the ventricles.

Fig. 276.—Tuberculoma in the medulla of a child.

The new growth may appear to originate in the meninges, it may be secondary to a tumor in the brain or cord, or, as in a case of melanotic sarcoma which I studied, it may arise outside the central nervous system. In this case the primary growth was a melanoma of the skin of the back, the entire brain was covered by a thin yellowish-brown layer composed of pigmented cells which invaded the perivascular lymph spaces and thus penetrated for some little distance into the cerebral substance, and the cerebrospinal fluid contained numerous large pale cells. By recognition of these cells it is possible to make a diagnosis during life. The symptoms are those of chronic meningitis. Our own case was first regarded as epidemic encephalitis and then as syphilitic meningitis.

Tuberculoma.—The large solitary tubercle is a peculiar manifestation of tuberculosis in such organs as the brain and liver where the extension of the inflammatory process is allowed to proceed symmetrically, unhampered by planes of fascia or strands of connective tissue. Occurring usually in children, it is frequently multiple, and may attain to the size of a walnut. It is most often found in the cerebellum, the cerebrum coming next in frequency. It forms a firm, well-defined, spherical mass which may readily be mistaken for a true tumor, although if softening occurs it may resemble an abscess. Of the three specimens in the University of Manitoba Pathological Museum one is usually taken for a tumor, the other two for an abscess.

Gumma.—Gummata usually originate in the meninges and invade the brain secondarily. The tumor is grey or reddish-grey in color, somewhat irregular in outline, and of fine consistence, although necrosis and softening may occur later. Eventually it becomes replaced by fibrous tissue, tell-tale scars remain, and the meninges are adherent to the surface of the brain.

Pseudo-tumor Cerebri.—Under this name, which is clinical rather than pathological, are included certain cases which present the cardinal symptoms of cerebral tumor, but in which the clinical course disproves the diagnosis. Many pathological lesions may give rise to symptoms which simulate cerebral tumor. Scattered amongst the literature are to be found cases resembling tumor cerebri in which the underlying condition was cerebral syphilis, atypical tuberculous connective tissue changes, meningo-encephalitis, and basal meningitis. In many of the cases there has been an abundant serous exudate in the brain. Quincke describes a chronic form of serous meningitis which may for years have the aspect of a slowly growing brain tumor. Cushing uses the term arachnoiditis to denote a somewhat similar condition. In a case recently studied in the Winnipeg General Hospital the final (probable) diagnosis arrived at was encephalitis lethargica after the patient had narrowly escaped an operation for cerebello-pontine angle tumor; recovery in this case was complete.

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CHAPTER XXXII

THE PITUITARY BODY

It sometimes happens that the physiologist, by throwing light on the function of an organ, attracts the attention of the surgeon to that part. Perhaps quite as frequently the process has been reversed. Of this the pituitary is an excellent example. It was the gross lesions of this small structure which first attracted attention, and only then was it realized what a wealth of interesting information regarding its function was lying there waiting to be extracted.

The pituitary body, like the adrenal, consists of two parts which differ absolutely in structure, in function, and in development.

Structure.—The anterior part is glandular in structure, and is developed as an upgrowth of the pharyngeal epithelium known as Rathke's pouch. The stalk connecting this part of the pituitary with the pharynx disappears, but portions or embryonal rests may remain, and from these rests rare tumors, usually squamous-celled carcinomata, may develop in any portion of the vestigeal track. The anterior part clothes and envelopes the posterior part in very much the same way as a hand holds a cricket ball (Cushing).

The posterior part, of nervous structure, is developed as a downgrowth from the floor of the third ventricle, and remains connected with its site of origin by a slender stalk or infundibulum. In the lower animals a wide space persists in the posterior part, but in man all that remains of the communication with the ventricle is a very narrow channel in the infundibulum. Even this, however, may be of importance, for both Herring and Cushing, the one on anatomical, the other on experimental grounds, consider that along this channel passes the secretion of the pituitary gland, which thus reaches the third ventricle and the cerebrospinal fluid, and so is finally absorbed.

The pars intermedia, frequently referred to in physiological writings, is an investment of epithelium which clothes the posterior portion and which constitutes a special lining for the gap which partially separates the anterior and posterior parts.

The anterior part is made up of columns of cells surrounded by large blood sinuses. These cells are of two main types; chromophil and chromophobe. The former, which are by far the more numerous, have a granular cytoplasm which stains deeply; the latter, often known as the chief cells, which are few in number under normal conditions, are of small size and possess a scanty cytoplasm which stains faintly. The chromophil cells may again be divided into eosinophil (or acidophil) and basophil, according to the staining reac-

tion of the granules. The eosinophil cells are more abundant at the center of the gland where they line the blood sinuses, the basophils are more numerous at the periphery.

Whether these three types represent distinct kinds of cells or whether they should merely be regarded as different phases of the same cell is at present a moot point. It seems probable that the latter is the correct view. The eosinophils appear to be the elements which produce the internal secretion under normal conditions. They line the blood channels, and their secretion is absorbed into the blood stream. If this absorption does not occur the eosinophil gradually becomes converted into a basophil. In time the basophil discharges dark basophil colloid, and becomes changed into a small shrunken chromophobe cell. Eventually the small chromophobe once more develops into an eosinophil. Should there happen to be an urgent demand for pituitary secretion, as in pregnancy, the small chromophobes increase in size but remain chromophobe, and yield up their secretion as soon as formed.

Blair Bell summarizes the process as follows: "The small chromophobe cells are exhausted cells; the eosinophil cells are the active secretory cells in normal circumstances; the basophil cells form a storage secretion; and the large chromophobe cells, which develop from the small exhausted chromophobe cells, are formed only where there is an urgent and immediate need for the secretion of the pars anterior."

Although the usual arrangement has just been described, the entire picture may change when the gland is subjected to any physiological stress. This is best seen in pregnancy, when the eosinophils become almost entirely replaced by the chief or chromophobe cells. Experimental extirpation of a portion of the anterior lobe and infections of various kinds may result in a similar hyperplasia of the chief cells. The colored frontispiece to Cushing's book shows this change in a very striking manner.

The pars intermedia is the thin epithelial investment of the posterior part, which becomes thickened at the anterior end of the infundibulum where it fuses with the anterior part. Under some conditions its cells become arranged to surround acini which contain colloid, and this colloid material has been traced by Herring back through the posterior portion into the infundibulum.

The posterior portion is singularly uninteresting in its structure. No nervous elements can be distinguished, and it is composed of a mass of neuroglia with here and there a few small cells. No one would suspect from a study of this inert-looking structure that an extract prepared from it was capable of producing the most dramatic physiological results.

The *weight* of the pituitary presents one point of great interest, for it is heavier in adult parous females, especially multiparæ, than in nulliparæ and in males. Halliburton, Candler, and Sykes examined the pituitary in 18 adult males; in only 4 cases did it weigh more than

0.5 gm. and the average was 0.46 gm. In 24 females, on the other hand, the average was 0.56 gm., and in only 4 cases did the gland weigh less than 5 gm. In pregnancy it may be 0.75 gm. or more.

Physiology.—The physiology of the pituitary is still far from being an open book, but much light has been thrown on the subject by a study of the pathological disturbances to which the gland is liable.

At the very outset we are faced by one remarkable fact. The anterior portion is to every appearance the active part of the gland, being made up of different kinds of epithelial cells which vary in their proportion under different physiological conditions, and yet an extract of this part is absolutely without any physiological effect. On the other hand the extract of the inert-looking posterior lobe produces the most startling results. This substance excites a contraction of plain muscle throughout the body, raises the blood pressure to a marked degree through a general arterial contraction (but relaxes the renal vessels, thus producing diuresis), causes the uterus to contract violently, stimulates the secretion of milk, and, by greatly lowering the sugar tolerance, causes sugar to appear in the urine. It of course does not follow on that account that the normal function of the posterior lobe of the pituitary is to produce all or any of these peculiar physiological results.

From experimental results on animals the posterior lobe does not appear to be essential to life. Indeed the whole of it may be removed without producing any noticeable effect apart from polyuria, although it is possible that the resulting adiposity may be traced to this source.

Removal of the whole gland results in death from collapse in the course of a few days. When only a small portion of the anterior lobe is left the animal becomes very fat, sexual development does not proceed, and there is polyuria and a remarkable degree of sugar tolerance.

Although it is not possible accurately to separate the functions of the two portions of the gland we may say that the anterior part is concerned with growth, particulary the growth of the skeleton and the development of the sexual organs, whereas the posterior lobe appears to be concerned with carbohydrate metabolism and therefore with the development of fat.

An interesting feature which may be mentioned in passing is the development of diabetes insipidus, characterized by extreme polyuria and unslakable thirst, in some cases of pituitary tumor. The condition appears to be a deficiency disease, due to lack of the secretion of the posterior lobe. Administration of pituitary extract and lumbar puncture have both produced remarkable results in certain cases.

The *relation of the pituitary to the other ductless glands* is a subject regarding which little is definitely known, but that some such relationship exists is certain. In myxedema and cretinism there is a marked increase in the chromophobe cells and other evidences of pituitary activity. The same is observed in colloid goiter, and there may be a well-marked acinous arrangement of the cells with accumulation of colloid material in the acini. In exophthalmic goiter, on the other

hand, there is an equally great increase in the basophil cells, indicating a condition of inactivity. There may also be a relationship between the pituitary and the adrenal. Blair Bell, for instance, shows an illustration of a case of combined Addison's disease and acromegaly. Removal of most of the adrenal tissue is followed by pituitary hyperplasia. The connection between the pituitary and the gonads is also of great interest. In women hyperpituitarism causes the immediate cessation of menstruation, followed shortly by the assumption of male secondary characteristics. In men, on the other hand, there is often increased sexuality. Hypopituitarism in both sexes is accompanied by genital hypoplasia. Partial removal of the anterior lobe of the pituitary leads to profound degeneration of the epithelium of the Graafian follicles, the ova, and the interstitial cells of the ovary.

Pathological processes affect the gland as a whole rather than its constituent parts, although the hyperplastic processes naturally commence in the glandular portion, but in unravelling the pathological symptomatology it is of value to keep in mind the principal functions of the two parts.

Reference has already been made to the remarkable physiological hyperplasia which the pituitary undergoes during pregnancy. In some cases the weight may be nearly doubled. The new tissue is made up of the chief or chromophobe cells, which are often arranged in definite adenomatous masses. These masses usually disappear with the termination of pregnancy, but transitions to atypical adenomata of malignant type have been observed. As already pointed out, the weight of the pituitary is distinctly greater in multiparæ than in nulliparæ.

Pathology.—If the physiology of the pituitary is confused, the pathology is even more so. Certain definite symptom-complexes have come to be recognized as pituitary in origin, but there is no uniform underlying pathology.

The pathological manifestations of pituitary disorder may conveniently be grouped under the headings of hyperactivity and hypoactivity. Again it is difficult to separate the two parts of the gland as regards activity of function, but when we speak of the pituitary being overactive it may be assumed that it is the anterior portion which is at fault. In each case the result depends on whether the disease commenced before skeletal and sexual development was completed or after that period. There are therefore the following possibilities.

1. *Hyperactivity before ossification is completed* invariably results in some degree of *gigantism*. Every giant at some stage shows hyperplasia of the pituitary. This, however, at once introduces us to the fact that pure pituitary lesions are rare. Hyperfunction is often followed by or even associated with hypofunction. A giant frequently shows symptoms of hypopituitarism such as a high sugar tolerance or sexual impotence. If the activity of the pituitary is maintained there will be a low sugar tolerance and glycosuria. Many giants die of diabetes.

The condition of the pituitary corresponds with the clinical symptoms. When hyperfunction is still in evidence the pituitary may be found to be much enlarged, and the sella turcica shows a corresponding expansion which can often be readily recognized by means of X-ray pictures. Erosion of the posterior clinoid processes is a feature specially worthy of note. Later in the disease the pituitary may be greatly shrunken or converted into a cyst, but the tell-tale bony changes bear evidence to the former hyperplasia.

2. *Hyperactivity after ossification is complete* results in *acromegaly* (enlargement of the extremities). This condition, first recognized by Pierre Marie in 1886 to be due to disorder of the pituitary body, is characterized by great enlargement of the hands and feet, the bones of the face, and the lower jaw. Both the bones and the soft parts of the hands and feet participate in the enlargement. Symptoms of gigantism may be present, indicating that the period of pituitary overactivity has antedated the cessation of ossification.

The diagnosis of acromegaly is readily made when the changes are at all pronounced. The face is large, the frontal sinuses prominent, the eyes deeply set, the lower jaw is heavily undershot and prognathous so that the lower teeth project beyond the upper ones, the teeth themselves are widely separated (a very constant sign of the disease), the lips are thick and the tongue hypertrophied, the skin is thick and deeply furrowed, the hands and feet are huge, clumsy, and boggy, the enlargement being one of the soft parts rather than of the bones. One of the most characteristic features is the presence of exostoses on the phalanges of the fingers, and in particular a tufting of the terminal phalanx. This forms a striking picture on the X-ray plate.

The disease is self limited, and sooner or later the symptoms of hyperpituitarism are succeeded by those of hypopituitarism. Of the latter, adiposity, somnolence, sexual impotence, and high sugar tolerance are the most important. Cases of acromegaly when seen in actual practice have usually left the active stage behind, and show well marked signs of pituitary insufficiency.

The *pathological changes* in the pituitary during the active stage of acromegaly are a hyperplasia of the eosinophil cells of the anterior part. This hyperplasia may be diffuse, but usually it is so localized that it may be termed adenomatous. The swelling of the gland results in absorption of the bone of the sella and upward distension of its membranous roof. The now well-recognized pituitary type of headache is due to a similar enlargement of the gland, but much less marked in degree; such cases may be examples of work hypertrophy, for they are often relieved by the administration of pituitary extract. In one case of Erdheim's the pituitary was normal, but there was an acidophil adenomatous tumor of an accessory gland in the sphenoidal cells. Although most writers consider that the eosinophils are the important cells in acromegaly, Cushing found what he calls a chromophobe struma in most of his cases. Later in the disease when symptoms of

pituitary insufficiency have begun to manifest themselves the gland may be found atrophic or cystic.

3. *Hypoactivity of the Pituitary. Fröhlich's Syndrome.*—When this occurs in early life the result is a condition of infantilism in which there is a notable absence of development of the skeleton and the sexual glands, and the secondary sexual characteristics do not appear. In addition to these anterior lobe symptoms there develop great obesity and a high sugar tolerance, which may be ascribed to the posterior lobe. These bodily changes are quite in keeping with the remarkable condition of mental torpor into which the patient appears to be plunged. The fat boy fairly bursting from his clothes and ready to sink into slumber at a moment's notice has been drawn for all time in the immortal pages of Pickwick.

This peculiar condition of adiposity combined with lack of sexual development is known as dystrophia adipososexualis or Fröhlich's syndrome. It was first recognized in man by Fröhlich in 1901, but it was a great step in advance when Cushing in 1909 was able to produce a similar condition in young animals by removal of the posterior lobe and the greater part of the anterior lobe of the pituitary.

When the insufficiency develops after puberty the skeleton and the sexual organs will be fully formed, but the characteristic adiposity, torpor, and high sugar tolerance appear as before, and the deposit of fat in the breast and hip regions will often give the man a distinctly feminine cast of figure.

No one *pathological lesion* is found in all these cases of pituitary insufficiency. Lesions both of the gland itself and of structures in its neighborhood may give rise to an insufficiency syndrome. There is a specimen in the Pathological Museum of the University of Manitoba showing a tumor (a glioma) encircling the infundibulum but leaving the pituitary itself quite intact. The patient, who was under the care of Dr. Harvey Cushing, was considered to be suffering from symptoms of pituitary insufficiency. Such a case would appear to support the idea that some at least of the secretion of the gland passes to the third ventricle via the infundibulum, there to be absorbed. In another case, kindly shown to me by Dr. A. T. Mathers, very definite symptoms of pituitary insufficiency came on a few months after a characteristic attack of epidemic encephalitis. The pathological substratum therefore evidently varies widely in character.

In the majority of cases, however, the lesion found at operation or autopsy is a definite tumor or overgrowth to which Cushing gives the somewhat unsatisfactory name of struma. This is composed of the chief or chromophobe cells, similar to those which appear so abundantly during pregnancy.

PITUITARY TUMORS

Tumors of the pituitary body proper may be divided into: (1) hyperplasia, whether diffuse or focal, and (2) carcinoma. In addition to these tumors of the gland we must consider those tumors which

arise along the track of development of the anterior lobe of the pituitary from the bucco-pharyngeal cavity.

1. **Hyperplasia.**—Overgrowth of the anterior part of the pituitary is of fairly common occurrence. It is a constant accompaniment of pregnancy, but when the pregnancy terminates the hyperplasia usually disappears. Cases have been recorded in which the hyperplastic gland has reached the extraordinary weight of 1.65 gm. The hyperplasia may be diffuse, or it may be distinctly nodular, so that definite adenomata are formed. The latter appear to come legitimately within the realm of true tumors, but with regard to the former it is difficult to express an opinion. The effect of these hyperplasias or strumas upon the immediate surroundings of the pituitary has already been discussed.

In acromegaly the lesion is often merely a simple hyperplasia, either diffuse or adenomatous. As a rule it greatly exceeds anything found in pregnancy, but in some cases the changes have been remarkably slight. Eosinophil cells are usually in marked preponderance, but Cushing has reported a number of cases where the tumor has consisted chiefly of chromophobe cells. In still other cases of acromegaly and gigantism basophilic adenomas have been described. This is a good example of the confusion of pituitary pathology at the present time.

2. **Carcinoma.**—Ewing is of the opinion that all true tumors of the pituitary, as opposed to simple hyperplasia, are malignant in nature. The tumors may be regarded as adenocarcinomata. At first the tumor is purely intrasellar. As it grows it causes enlargement of the sella and absorption of the clinoid processes; the roof of the sella is burst and the tumor may invade the floor of the third ventricle. Any of the surrounding structures may suffer extensively. In one case which I studied the patient had marked cerebrospinal rhinorrhea; whenever he sat up in bed cerebrospinal fluid dropped from his left nostril. At the autopsy it was found that the entire floor of the sella had been destroyed by a carcinoma of the pituitary, and that a free communication existed between the cranial cavity and the nose.

The *microscopic picture* consists of irregular groups or solid cords of cells separated by abundant blood vessels. The cellular arrangement is atypical; sometimes the cells surround acini which contain colloid, and in such cases cystic degeneration is not uncommon. As a rule the cells are entirely chromophobe, but in some of the less malignant varieties chromophil cells have been present in small numbers.

In the literature descriptions of sarcoma of the pituitary are frequently encountered. It is probable that no such condition exists. Most of the cases are examples of adenocarcinoma; in some instances a nodular chromophobe hyperplasia has been mistaken for sarcoma.

The *symptoms* of pituitary tumor fall into three main groups: (1) those of cerebral tumor in general, notably high intracranial pressure; (2) neighborhood symptoms; and (3) symptoms of pituitary insufficiency. It is not necessary to go into these in detail, but it

may be mentioned with regard to neighborhood symptoms that the optic atrophy due to direct pressure on the nerve is primary in type, not the usual atrophy secondary to an optic neuritis which is seen in ordinary cases of cerebral tumor, and that pressure on the inner fibers of the optic chiasma may readily give rise to a homonomous hemianopia.

The evidence of pituitary disturbance has already been discussed. Much will depend on whether the onset is before or after puberty. In the case of carcinoma the disturbance will always be in the direction of insufficiency. The tumors of chromophobe cells also give rise to insufficiency symptoms, but, as we have already seen, the chromophil hyperplasias may be associated with symptoms of pituitary hyperfunction.

Tumors of the Hypophyseal Duct.—At any point in the course of the primitive duct, extending from Rathke's pouch to the floor of the sella, tumors may develop from vestigeal remnants.

The most common variety is the *epidermoid carcinoma* or epithelioma, although even it is very rare. It originates from the epithelium of the bucco-pharyngeal cavity, but is most frequently found within the sella. The stratified epithelium often surrounds cyst-like spaces.

Dermoid tumors may occur in the same neighborhood, and owe their origin to invagination of the cranial epidermis during the closure of the neural canal.

Simple cysts may develop from distension of Rathke's pouch. They are filled with serous fluid, and usually lie between the anterior and posterior lobes.

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CHAPTER XXXIII

THE SPINE AND SPINAL CORD

SPINA BIFIDA

Spina bifida is a congenital defect due to failure of the neural arches to close, and accompanied by a protrusion of the contents of the spinal canal. As normally the lower part of the canal is the last to close, spina bifida is commonest in the lumbo-sacral region, although any part of the spine may be affected. As a rule about five or six vertebræ are involved, sometimes only one, very rarely the entire column. The condition is fairly common, occurring about once in every 1000 births.

The contents of the sac may be of three varieties: (1) a meningocele, (2) a meningo-myelocele, and (3) a syringo-myelocele.

Meningocele.—This usually occurs in the sacral region. It consists of a sac composed of the dura and arachnoid and is filled with cerebrospinal fluid, but contains no nervous structures. At birth it is usually not larger than a hen's egg, but it may rapidly increase in size. It frequently becomes pedunculated. The skin is usually normal at first, but becomes thinned as the cyst increases in size, and may finally give way.

Meningo-myelocele.—In this condition, which is the commonest form of spina bifida, and which usually occurs in the lumbar region, the sac contains the spinal cord or the cauda equina in addition to the cerebrospinal fluid. The cord may pass straight back into the sac and end by becoming attached to its wall. If the defect is higher up the cord may enter and leave the sac. The cord and the nerves are usually flattened and frequently attached to the wall of the sac, producing a dimple known as the umbilicus. The sac is sessile, and the overlying skin is so thin that, by means of illumination, it may serve to distinguish the condition from a meningocele. A meningo-myelocele is naturally a much more serious condition than a simple meningocele.

Syringo-myelocele.—This is a rare form of spina bifida in which there is a great distension of the central canal with consequent thinning of the nervous tissue of the cord. The wall of the sac is therefore actually lined by the thinned wall of the canal. The condition is apt to be mistaken for a meningocele, because at first sight no nerves are evident in the sac. Closer inspection will disclose the nerves incorporated in the wall of the sac, that is to say in the distended cord.

The various forms of spina bifida are frequently accompanied by complications. The most significant of these is congenital hydro-

cephalus, for it suggests a causal relationship between the two conditions. Other accompaniments are paralysis of the bladder and rectum, weakness in the muscles of the legs leading to club-foot, trophic ulcers, etc., due to pressure on the nerve centers. When the lesion is in the sacral region there may be no nervous disturbances.

The *prognosis* is bad. Early death is the best termination. Not many cases live beyond the age of four or five. Death is usually due to rupture of the sac or the development of septic meningitis, but occasionally it is due to hydrocephalus.

Spina Bifida Occulta.—In this form of spina bifida the bony defect is not accompanied by any protrusion of the contents of the spinal canal. It follows that it is neither so easily recognized nor so liable to produce symptoms.

Its presence is usually revealed by the character of the skin covering the bony defect, for this is rough and wrinkled and adorned with a patch of hair which may occasionally resemble a small tail. The opening in the bone can usually be felt, or it may be best revealed by means of the X-rays.

Small tumors, of which the commonest are lipomata and dermoids, may occur either inside or outside the canal. In the latter case they project under the skin. They are developmental in origin, and are due to the growth of embryonal cells which continue their activity after the formation of the defect.

There may be no symptoms, or there may be paralysis of the legs and the sphincters, club-foot, the development of trophic ulcers, and other symptoms difficult of explanation until the spina bifida is discovered. The symptoms are usually due to a tough cord of connective tissue stretching from the skin through the vertebral defect and attached to the termination of the cord, on which it exerts traction with the production of nervous symptoms. The traction is due to the fact that the vertebral column grows at a faster rate than the connecting strand, and as the chief period of growth is between the ninth and fifteenth years, it is at this time that the symptoms are most likely to appear.

CONGENITAL SACRAL TUMORS

Although not related in any way to spina bifida, certain peculiar sacral tumors may be considered here, as they also are congenital in origin. These tumors may be divided into three groups: dermoid cysts, sacral cysts, and coccygeal cysts.

Dermoid cysts occur in the middle line over the sacrum, and usually contain the characteristic sebaceous material, hair, and teeth. Instead of a typical dermoid cyst there may, in rare cases, be anything from a lower limb up to a more or less fully formed fetus. The simpler cysts are formed by the inclusion of epithelium in the closure of the vertebral groove, but the more complex masses are supposed to originate from the formation of two embryonic areas in a single developing blasto-

dermic vesicle, the one giving rise to the normal individual, the other to the parasitic fetus.

Sacral cysts are cystic, sessile masses containing serous fluid and lined by endothelium. Their exact origin is not certain, but it has been suggested that they represent a sacral meningocele which has been cut off by the continued growth of the vertebral arches.

Coccygeal cysts are placed laterally, thus being distinguished from the two former varieties. Moreover they are situated deeply among the gluteal muscles. They have been thought to arise from the post-anal gut, that is to say the neurenteric canal.

FRACTURES OF THE SPINE

Fracture of the spine is of special interest in view of the possibility of injury to the cord. The spines, the laminæ, or the transverse proc-

FIG. 277.—Fracture-dislocation of spine with severance of cord.

esses may be fractured, but two varieties of fracture deserve special mention, namely compression fracture of the bodies of the vertebræ and fracture-dislocation.

In *compression fracture* of the bodies there is crushing of the bodies of one or more vertebræ owing to the patient falling from a height and

landing on his buttocks or his feet. As there is no dislocation there is very little deformity, and usually no laceration of the cord. The bodies being crushed in, there is some projection of the spines.

In *fracture-dislocation* there is complete bilateral dislocation of the articular processes together with an oblique fracture downwards and forwards of one or more of the vertebræ. The effect on the cord is instantaneous and disastrous, for the upper fragment moves forwards and downwards, nipping the cord and crushing it irretrievably.

POTT'S DISEASE OF THE SPINE

Of the "big four" diseases in relation to the spine, inflammation, tuberculosis, syphilis, and tumors, tuberculosis so far transcends the others in importance that it will be considered first.

FIG. 278.—X-ray picture of tuberculosis of the spine (central form). There is marked destruction and collapse of the bodies of the vertebræ.

The disease was first described by Percival Pott in 1779, and has since that time been known by his name. It is much commoner in children, but is not infrequent in adults. The dorso-lumbar region of the spine is most frequently involved.

The disease as it occurs in children differs somewhat from that which affects adults. The former commences as an osteomyelitis, the latter as a periostitis.

Tuberculous osteomyelitis begins in the cancellous tissue of the body of a vertebra, usually towards the anterior surface. By means of a slow and insidious caries the bone is eaten away and replaced by tuberculous granulation tissue, which in turn becomes softened with

Fig. 279.—Tuberculosis of spine: extensive periosteal involvement; no deformity.

the formation of caseous purulent material. The disease spreads to the intervertebral cartilages, but leaves the transverse processes, spines, and articular processes unaffected. The intervertebral articulations, therefore, remain intact whilst the anterior part of the bodies are being

eaten away. The result is that the bodies collapse in front but the spines remain intact behind, so that an acute curvature with its convexity pointing backwards must inevitably develop.

Tuberculous periostitis is the form usually found in the adult. It differs from the central variety in three particulars. (1) It is naturally a more diffuse process, so that half a dozen vertebræ may be involved. (2) Owing to the absence of extensive destruction in the vertebral bodies there is much less deformity, what deformity there is being rather a gentle curve than an acute angle. (3) The process

FIG. 280.—X-ray picture of tuberculosis of the spine, both central and periosteal. The anterior surface of all 12 dorsal vertebræ is affected.

being a superficial one, abscess formation is commoner and occurs at an earlier date.

The *course* of the disease is variable. Owing to the constant movement of the parts there is a strong tendency to progression. If, however, the patient is placed absolutely at rest and in the best hygienic surroundings there is an almost equally strong tendency towards repair, the tuberculous granulation tissue becoming fibrosed

and the vertebræ bound together by fibrous adhesions which ensure firm fixation.

Pressure Effects.—In most cases, especially in children, there is evidence of pressure on the cord. This is rarely due to the angling of the spine or narrowing of the canal; indeed the intact condition of the articulations prevents such narrowing from attaining any marked degree. The pressure is due to edema of the soft parts, to the formation of a mass of tuberculous granulation tissue, and to an accumulation of pus under the posterior common ligament compressing the cord. An accompanying *myelitis* may intensify the nervous symptoms. The motor fibers, lying as they do in the antero-lateral region of the cord,

Fig. 281.—Pott's disease of the spine. (MacCallum.)

are the first to suffer, so that first there may be a slight weakness but later a severe degree of paraplegia of the spastic type. As a rule there are few or no sensory changes, but should myelitis develop there will be complete loss of sensation below the level of the lesion. It is remarkable, however, to what extent the pressure symptoms may clear up when the weight is taken off the spine, even when there has been quite a severe degree of paraplegia.

Abscess Formation.—The tuberculous pus formed at the seat of the disease displays a remarkable tendency to travel. The posterior common ligament provides an obstacle to its direct spread backwards,

but it soon escapes at the sides of the vertebræ, and passes either backwards or forwards.

It may pass backwards along the posterior branches of the intercostal nerves and vessels, with the formation of a dorsal or lumbar abscess.

If it passes forward the result will depend on the part of the spine affected. In the *cervical region* it will accumulate between the vertebræ and the wall of the pharynx to form a retropharyngeal abscess, which may first bulge and finally burst into the pharynx, or may appear

Fig. 282.—Healed tuberculous spine, the result of a Hibbs' operation.

at the side of the neck behind the posterior border of the sternomastoid. The latter course is the more common, for the prevertebral fascia usually prevents it from entering the pharynx.

In the *upper dorsal region* the pus may spread forward between the ribs and the pleura, coming to the surface along the lateral cutaneous branches of the intercostal nerves, and forming an abscess over the middle of the rib, which is very apt to be mistaken for tuberculous disease of the rib. In every case of cold abscess of the rib the spine

must be carefully examined. Occasionally a mediastinal abscess may form, which may press on the trachea but usually gives rise to no symptoms.

In the *dorso-lumbar region* the pus enters the sheath of the psoas muscle, and passing down as a psoas abscess into the iliac fossa and under Poupart's ligament, it may appear at the saphenous opening, or at some point further down the thigh. In some cases the pus may enter the sheath of the iliacus instead of the psoas, in which case it will either point above Poupart's ligament or pass down into the pelvis.

FIG. 283.—Tuberculous abscess secondary to Pott's disease of the spine. The abscess involved the cervical and the entire thoracic region. (From the same case as Fig. 279).

A tuberculous abscess may be present for a considerable time and yet produce extraordinarily few symptoms. At the same time the threat of mixed infection is always present, a threat which is certain to be carried into execution the moment the abscess discharges on the surface. The entire clinical picture then alters, and the patient dresents a hectic temperature, becomes rapidly emaciated, develops amyloid disease, and may die of general miliary tuberculosis.

OSTEOMYELITIS OF THE SPINE

Acute pyogenic inflammation of the vertebræ is commonest, as in the case of other bones, between the ages of 5 and 15, that is to say while the bone is still growing and vascular. The staphylococcus aureus is the chief causal germ.

The inflammation is commoner in the processes than in the bodies of the vertebræ, thus differing from tuberculosis. When it begins in the arches the pus spreads backwards, when it begins in the bodies it spreads forwards, and, following the example of tuberculosis, may give rise to retropharyngeal, mediastinal, and psoas abscesses. An extradural abscess may form which presses on the cord. Death results from septic meningitis.

Typhoid Spine.—During convalescence from typhoid fever, and occasionally during the course of the disease, an inflammation of the lower part of the spine may develop, associated with great pain and tenderness. As the disease is not fatal there have been no opportunities for post-mortem observations, but X-ray studies leave no room for doubt that the condition is a superficial osteomyelitis, unaccompanied except in rare cases by suppuration, and followed by new bone formation. X-ray pictures show roughening of the adjacent surfaces of the vertebræ; the intervertebral space becomes narrowed and finally obliterated; osteophytic outgrowths develop at a later date. In tuberculosis, on the other hand, new formation of bone is conspicuously absent.

SYPHILIS OF THE SPINE

Gummatous formation in the vertebræ may closely simulate Pott's disease. It is most common in the cervical region, the deformity is not marked because the destruction of the vertebral bodies is not extreme, there is no abscess formation, other signs of syphilis are present, the onset is more sudden and the progress more rapid than in tuberculosis, and the Wassermann reaction is positive.

TUMORS OF THE VERTEBRÆ

The usual tumors of bone may affect the vertebral column, but the only ones which call for special mention are sarcoma, myeloma, and secondary carcinoma. Tumors of the vertebræ are usually situated in the bodies.

Sarcoma of the spine is usually primary, but may be secondary. It causes pressure on the cord and may readily be mistaken for Pott's disease. The sacrum is the most common site, and there it may cause severe sciatica.

Multiple myelomata, when they do occur, are usually found in the sternum as well as in the spinal column, the cranium, and the long bones. Bence-Jones protein is present in the urine in 50 per cent of the cases.

Carcinoma secondary to malignant disease in such glands as the breast, the thyroid, and the prostate is by no means rare. Secondary deposits from a hypernephroma may also occur. The bodies of the vertebræ are destroyed, and a deformity suggesting that of Pott's disease may be produced. Pressure symptoms amounting to complete paralegia may develop with startling rapidity.

SPONDYLITIS DEFORMANS

The spine may be the seat of arthritis deformans, of which the great symptom is spinal rigidity. Formation of osteophytic outgrowths with consequent limitation of movement may occur in a number of diseases such as gonorrheal rheumatism, osteomyelitis, typhoid fever, etc. Apart from these, however, two groups of cases may be distinguished:

1. Those in which the vertebræ are locked together by bony outgrowths, and in which there is a tendency to bony hypertrophy. The condition is similar to osteo-arthritis occurring in other joints.

2. Those in which the various ligaments and joint capsules become ossified, but without the formation of osteophytes. Indeed there is rarefaction and fibrillation of the bodies of the vertebræ and the intervertebral discs.

The result in both cases is the same. The spine is converted into a rigid rod. Sometimes the column is straightened, so that there is a veritable poker back, particularly in the osto-arthritic variety. More usually the spine becomes rigid in a kyphotic position, so that the rigidity and deformity may suggest Pott's disease. The chest becomes flattened and fixed owing to ossification of the costo-vertebral ligaments.

Sensory symptoms in the shape of neuralgic pains and paresthesiæ are common but difficult of explanation, for at autopsy there is no narrowing of the intervertebral foramina to account for the pressure symptoms. Muscular spasms and some slight wasting also occur.

INJURIES OF THE SPINAL CORD

The spinal cord may be injured as the result of fracture of the spine, the most common cause; or from bullet or stab wounds; or from mere overstretching of the cord owing to acute flexion of the spine from a blow. The laceration of the cord may be complete, in which case there is immediate paralysis, both sensory and motor, of the entire body below the lesion. Or it may be partial, the varying symptoms depending on the site of the lesion.

Hemorrhage is a very constant accompaniment of spinal injuries. This hemorrhage may be extramedullary or intramedullary.

Extramedullary hemorrhage often gives rise to no symptoms of pressure on the cord, but in some cases there may be indications of pressure on the cauda equina, owing to the blood gravitating to the bottom of the arachnoid sac and accumulating there in sufficient amount to exert pressure. In the cases where symptoms of cord pressure at the site of the hemorrhage develop, the symptoms are at

first irritative in the form of muscular twitchings and root pains and only later paralytic. Moreover the onset of the symptoms is characteristically gradual. Blood in large amount is present in the spinal fluid.

Intramedullary hemorrhage or hematomyelia is always associated with more or less laceration of the cord. The hemorrhage, usually in the cervical region, is generally confined to the grey matter, but it may spread up and down for a considerable distance, so that the resulting paralysis may be correspondingly widespread. The symptoms are at once paralytic without any preliminary period of irritation. Moreover the onset is most abrupt. There may be no blood in the spinal fluid.

SPINAL CORD TUMORS

Tumors of the spinal cord are of more frequent occurrence than is commonly supposed; most of them are missed. The majority develop slowly, especially those of the extramedullary variety. The rapid development of symptoms as a rule indicates that the growth is a malignant one within the cord itself.

Although the cord is much compressed, generally from the side, it is remarkable how few pressure changes develop. It is for this reason that removal of these tumors is often attended with such satisfactory results. In some cases, however, there may be myelitis, hemorrhage and degeneration.

As Frazier remarks, there are three cycles in the life history of any spinal tumor. The first or root cycle is the longest, and the symptoms are unilateral in the early stage; there is first irritation and then compression of the nerve roots. The second cycle is characterized by the Brown-Séquard syndrome, with paralysis of motion and deep sensation on the side of the tumor, loss of pain and temperature sense on the opposite side. The syndrome is present in extramedullary but not intramedullary growths. The third cycle is one of paralysis of the organic reflexes (bladder and rectum) and the deep reflexes, together with vasomotor and trophic disturbance.

Tumors affecting the cord may be (1) extramedullary, (2) intramedullary.

Extramedullary Tumors.—These tumors seldom invade the cord, but give rise to irritation and compression of the nerve roots. There may be root symptoms long before there is any sign of pressure on the cord; sometimes the interval may be as long as several years. They are usually situated on the lateral or postero-lateral aspect of the cord, so that the anterior roots escape, and there may be no motor symptoms.

The tumor as a rule grows very slowly, and although it may exert great pressure degenerative changes are sometimes almost entirely lacking. In other cases there may be considerable softening of the cord, but this is due to interference with the circulation rather than to direct pressure.

The tumor is usually oval, with the long axis in the direction of the cord, but it seldom attains to a size larger than 2–5 c.m. in length. A striking feature when the laminæ are removed is the absence of pulsation in the tumor, whereas the cord above and below may show normal pulsation. It is common to find collections of cerebrospinal fluid above the tumor, and very little fluid may be obtainable by lumbar puncture.

The tumor may be extradural or intradural.

Extradural tumors arise from the outer surface of the dura, and are much less common than the intradural variety. The interval between the root symptoms and those of cord compression may be very long, because the tumor is free to grow in a longitudinal manner. These tumors are often *sarcomatous*, and may invade the vertebral column. Hydatid cysts have been found in this position.

Fig. 284.—Intradural tumor of the spinal cord.

Intradural tumors form the commonest variety of spinal cord tumors. They are by far the most suitable group for operation, being usually well encapsulated and easily removed. Two of the most favorable for operation are the *endothelioma* and the *fibroma*. Both are firm, encapsulated, and show no tendency to invade the cord. Intradural tumors have frequently been reported as sarcoma, but even such tumors show a curious reluctance to invade the cord, although they may seriously compress it.

Intramedullary Tumors.—These constituted 11 per cent of Frazier's cases. The sequence of symptoms is often the opposite of that seen in extramedullary tumors, for the first or root period may be entirely lacking, and the progress of the disease is much more rapid. The tumor is generally limited to the cord, and seldom invades the meninges or the spine. It extends up and down rather than horizontally, so that the overlying dura may appear normal. The characteristic absence of pulsation indicates the site of the lesion.

The *glioma* is the common intramedullary tumor. It is a diffuse growth which may infiltrate large segments of the cord. Indeed Mallory describes a case in which a glioma originating in the lower part of the cord spread upwards till it reached and passed through the foramen magnum, and continued its course over the surface of the brain. A glioma may, however, be circumscribed and even

encapsulated. The cyst formation so often seen in the brain is rarely met with in the cord.

Sarcoma of the cord is a rare condition. A solitary *tubercle* of the cord will produce all the symptoms of a neoplasm. *Gummata* occasionally occur in the cord, but are much commoner in the meninges.

Cerebrospinal fluid changes are sometimes of great diagnostic value, not so much for determining the site and nature of the tumor as for detecting the presence of some process causing compression. The "compression syndrome" when fully fledged consists of the following: (1) massive spontaneous coagulation of the fluid due to an excess of fibrinogen; (2) xanthochromia or yellow coloration of the fluid; (3) marked increase in the protein; and (4) no corresponding increase in the cells, although if meningeal irritation is present there may be some lymphocytosis. The fully developed Froin syndrone is seldom seen, but the protein increase without a corresponding lymphocytosis is of common occurrence. It must be remembered, however, that any process which divides the spinal canal into a large upper compartment in communication with the cranial cavity and a small lower cul-de-sac will give rise to this condition. I have seen a case diagnosed from this test as one of spinal cord tumor which turned out at autopsy to be an example of Pott's disease with no deformity of the spine. On the other hand a tumor of the cord or the meninges which is not sufficiently large to obstruct the canal will produce no effect on the spinal fluid. With these exceptions the test is a very useful confirmatory one.

Specific tumor cells can sometimes be found in the fluid. This is particularly true of diffuse parcomatosis of the meninges.

Circumscribed Serous Meningitis.—Operations on the spinal cord have revealed a condition which may so closely simulate a spinal cord tumor as to deceive the very elect. A cyst-like space of varying size, containing clear cerebrospinal fluid, and limited by the arachnoid, is seen to be pressing on the cord which has a shrunken appearance. The fluid is under marked tension. The condition appears to commence in the lower part of the cord, and to spread up as far as the mid-dorsal region. The exact cause is unknown, although syphilis, trauma, and the other factors usually invoked in obscure neurological conditions, have all been cited. It may be that a mild meningitis has given rise to adhesions which, by cutting off a portion of the subarachnoid space, are responsible for the condition. The symptoms are those of an extramedullary tumor.

Reference for Further Study

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CHAPTER XXXIV

DISEASES OF BONES

GENERAL CONSIDERATIONS

Without attempting to give a detailed description of the structure of bone, a few anatomical points may be recalled with advantage. Bone is merely a form of connective tissue in which lime salts are deposited in the ground substance. The connective tissue is collected into strands or lamellæ between which there may be interspaces occupied by the marrow. Bone is described as compact or cancellous, depending on the amount of interspaces which it possesses.

A long bone consists of a shaft or diaphysis and two extremities or epiphyses, separated from the shaft by the epiphyseal cartilage and themselves covered by hyaline articular cartilage. That part of the shaft which abuts on the epiphyseal cartilage is of special importance in pathology and is called the metaphysis. It, like the epiphysis, consists of cancellous bone, the interstices of which are filled with red marrow. The epiphyseal cartilages at the knee are more active and become ossified later than those at the hip and ankle. In the upper limb it is the cartilages at the shoulder and wrist which are especially active. It may be noted here that inflammatory processes in the leg are common at the knee, in the arm they are commoner at the shoulder and wrist.

The Periosteum.—The periosteum constitutes the external covering of the bone, loosely attached to it except in the epiphyseal region through the medium of a delicate areolar tissue. In the interstices of this areolar tissue may be seen large cells whose function is osteogenic. These are the osteoblasts. They are abundant in the growing bone, but scanty in the adult. These cells have always been regarded as belonging to the periosteum, and that layer has been considered to be essentially osteogenic in function. Histologists describe the periosteum as consisting of two layers, an outer or fibrous layer and a deep or esteogenic layer.

In 1912, however, Macewen showed that this view was unsound, and that the osteoblasts belong to the cortex of the bone and not to the periosteum. When the periosteum is carefully raised and a subperiosteal resection of the bone is done no new bone will be formed from the periosteum unless a sharp instrument has been used so that some of the cortex comes away with the periosteum. On the other hand when a portion of bone deprived of its periosteum but retaining its osteogenic layer is transplanted to another part, new bone will be formed from the cortex. Gallie and Robertson have repeated this work with identical

results. The practical importance of this change of view and its bearing on bone surgery is self-evident.

New bone formation is an important feature in many pathological conditions. The repair of a fracture is brought about by the rapid proliferation of the osteoblasts, which together with the new capillaries form a granulation tissue which is converted into osteoid tissue and then into bone. This repair is not dependent on the periosteum. Indeed Macewen has shown that if a fracture is produced in a bone from which the periosteum has first been removed the formation of new bone (callus) will be more abundant than under ordinary conditions. In osteomyelitis the involucrum or new case is formed by the proliferating fibroblasts. It is true that here, as in the bone production which follows the subperiosteal hemorrhage of infantile scurvy, the new bone may be formed under the periosteum as well as on the surface of the shaft, but this is to be explained by the enormous proliferation which the osteoblasts undergo in the early stages of the irritation so that when separation of the periosteum occurs many osteoblasts are carried up with it. As a matter of fact subperiosteal resection is most likely to prove successful and to be followed by a complete restoration of bone in cases where previous inflammation has led to marked proliferation of the osteoblasts and commencing new bone formation.

Although recent work has deprived the periosteum of its osteogenic function, it nevertheless remains a structure of the greatest importance, for the bone is dependent on the periosteum for the greater part of its nourishment. If the periosteum is stripped from the shaft, or raised from it by an effusion the underlying bone will die. If no bacteria are present, as in the case of infantile scurvy, there may be no clinical evidence of the occurrence of necrosis, for the necrosed bone is quietly absorbed and replaced by new bone. If such necrosis should occur in the presence of sepsis, however, the result will be very different —an osteomyelitis of indefinite duration and the formation of a sequestrum.

The periosteum is easily separated from the underlying bone, so that inflammation may readily spread along the space between the two structures. When the periosteum reaches the epiphyseal cartilage the outer layer is continued on over the epiphysis, but the inner becomes fused with the epiphyseal cartilage. Pus under the periosteum, therefore, has difficulty in reaching the epiphysis and the corresponding joint.

The *blood supply* is of great importance. The outer layers of a long bone are nourished by the periosteum, the inner layer by the medulla. The intervening compact bone requires a special arrangement. Blood vessels run longitudinally through the bone in a series of channels called the Haversian canals, around which the bony lamellæ are grouped. Another series of vessels passes from the periosteum into the interior of the bone along Volkmann's canals. The nutrient artery enters the bone about the middle of the shaft and immediately divides into two branches, one of which passes in each direction and terminates

at the metaphysis in abrupt hair-pin bands. In this region we may expect the blood stream to be at its slowest, and it is here that organisms will be most likely to fall out of the stream. The epiphysis is supplied from vessels which anastomose around the joint from three sets of vessels, the diaphyseal, the metaphyseal and the epiphyseal, and thus epiphyseal vessels communicate with those in the metaphysis.

The Transplantation of Bone.—The fate of a bone which is transplanted from one part of the body to another or from one body to another is of great practical importance. When a bone is transplanted to another position the greater part of it dies. That the bone cells are necrosed is evidenced by their shrunken appearance in the lacunæ, which in many instances appear to be quite empty. But not all the bone cells share this fate; only those which are totally cut off from a supply of nourishment. Those which are still bathed by the lymph and body fluids continue to live, and these are the all-important bone-forming cells on the surface, lining the medullary cavity, and at the mouths of the Haversian canals. These osteoblasts, especially those lining the medullary cavity, show marked proliferation in the course of a few days. The cut ends of the graft show much less activity. Only the cells at the opening of the Haversian canals proliferate, and if there are no such openings there is no new bone formation.

The next step, as Gallie and Robertson have shown, is a vascularization of the necrosed bone. New vessels grow in from the surrounding tissues, make their way along the Haversian canal, and revascularize the bone. At the same time the proliferating osteoblasts accompany the new vessels, giant cells make their appearance, and the dead bone becomes absorbed by these cells and converted into a series of spaces lined by osteoblasts. These cells now commence the formation of new bone. The graft thus becomes absorbed and at the same time replaced.

These changes are entirely dependent on the activity of the osteoblasts. If the graft is first boiled and the osteoblasts killed, the graft will be vascularized, but neither absorption nor new bone formation will occur. If, however, the boiled bone is brought in contact with osteoblasts, it will be invaded in the same way as is the unboiled. Thus when only small gaps in healthy bone are to be bridged, as in the case of the spines of the vertebræ, boiled bone may be used, for the osteogenic tissue can completely invade the graft from the margins of the normal bone. Sepsis will effectually prevent all attempts at reconstruction, for the osteogenic cells of the surface are killed by the bacterial toxins.

The two processes are not evenly balanced. For the first six weeks or two months absorption proceeds more rapidly than new formation. If at the end of that period the bone has some function to perform, the process of absorption will give way to the process of reconstruction. On the other hand if the bone is implanted in muscle, where it has no work to, do the absorption process continues to have

the upper hand, until by the end of six months the graft is merely represented by a fibrous-tissue scar.

The activity of the osteogenic process will depend on the amount of surface with which the lymph can come into contact. In the case of cancellous bone such as rib, the reparation process will be much further advanced by a given date than when compact bone is used.

When a heterogenous graft is used, that is to say one from a different species, not only will the main body of the graft die, but also the osteogenic cells, for they do not find suitable nourishment in the lymph which bathes them. Even when a graft from another individual of the same species is used the properties of the nutritive fluids must be considered. It is known that skin grafts take better if the two persons concerned, the donor and the recipient, belong to the same blood group. The same may be true of bone grafts. If, therefore, the graft has to be taken from another person, it would be well to choose one belonging to the same blood group.

The four great diseases of bone are inflammation tuberculosis, syphilis, and tumors.

INFLAMMATION OF BONE

Inflammation of bone is merely a special example of the general process of inflammation. It is well to bear this in mind, for the anatomical peculiarities of bone have led to the use of a number of special names which are apt to convey the impression that we are dealing with something quite separate and apart. In the general chapter on inflammation we have seen that there are three possible courses which inflammation may take, resolution, suppuration with tissue death, and healing with fibrosis. This is true also for bone. But there are special factors which come into play. Tissue death is specially liable to occur because the nourishing periosteum may be lifted off the bone, because the unyielding nature of the tissue makes pressure from the inflammatory exudate inevitable, and because thrombosis of the vessels is of such common occurrence.

In bone, more perhaps than in any other tissue, the balance struck between the processes of destruction and repair is all important. If the infection is so slight that resolution occurs, no trace will be left of the struggle, although pain and other clinical phenomena may point unmistakably to its occurrence. If the infection is overwhelming death of the part will occur en masse, a process of *necrosis*, favored by the factors already mentioned, and comparable to sloughing or gangrene in soft tissues. The dead portion of bone which gradually becomes separated from the lining, is called a *sequestrum*, and imparts a characteristic gritty sensation to an examining probe.

Often, however, the balance is more evenly maintained, and an inflammatory granulation tissue is formed in the medulla, the Haversian canals, and the interstices between the laminæ, which exerts an eroding action on the hard bone with a resulting molecular death, rarefaction, or *caries*, so that the bone becomes, as it were,

worm-eaten; some parts are taken and others are left. The process, which corresponds to ulceration in soft tissues, may occur in subacute pyogenic infections, but is characteristic rather of the more slowly acting poisons of tuberculosis and syphilis. This same process of rarefaction it is which, acting around the margin of a mass of dead bone, gradually separates it from the living tissue and gives rise to a sequestrum. Much of the destructive action is carried on by osteoclasts, large phagocytic cells whose function in health it is to mould the growing bone in conjunction with the formative cells, the osteoblasts of the periosteum. Both necrosis and caries are manifestations, differing in degree, of the second variety of inflammation.

Healing with fibrosis in bone takes the form of sclerosis, a process of new bone formation in the cancellous spaces and in the walls of the Haversian canals, which may be slight in degree or may be so extreme as to dominate the whole picture. The new bone is denser than the old, and in that respect, as well as in the sites in which it occurs, it is abnormal. When a section of the shaft of a long bone dies it becomes surrounded by a layer of dense new bone called the *involucrum* or new case, which may be perforated here and there by tunnels called *cloacæ* running down to the sequestrum. When the lesion is more localized the reparative process may take the form of small spicules of bone projecting from the surface.

The balance between the forces of destruction and conservation may be such that a zone of densely sclerosed bone is formed around a small focus of softening in which bacteria may contrive to eke out an existence for many years. Such a circumscribed bone abscess is known as a *Brodie's abscess.*

It will thus be seen that there are four possible courses which pyogenic infection of bone may follow: (1) resolution; (2) a fulminating course; (3) the course of an ordinary osteomyelitis; (4) the formation of a Brodie's abscess.

The processes of destruction and sclerosis go hand in hand, but naturally the relative proportions vary greatly in different cases. In tuberculosis, in which caries is always well marked, sclerosis is seldom a prominent feature. In syphilis, on the other hand, the slowly acting spirochetes usually call forth an excessive amount of new formation.

The method of *spread* also varies in different infections. The suppuration of pyogenic infection readily passes through the open structure of the cancellous metaphysis, down the medullary cavity, along the surface under the periosteum, and from the surface to the marrow via the Haversian canals, so that it is doubtful if a pure infection of either the periosteum or the medulla can ever occur. The epiphyseal cartilage appears to present a formidable barrier to the spread of the infection, so that, even although the disease frequently commences in the metaphysis, infection of the joint is a comparatively rare occurrence. Tuberculosis behaves in

just the opposite manner. The process, again usually commencing in the metaphysis, remains fairly well localized with little tendency to spread down the medullary cavity, but invasion of the joint is the rule rather than the exception.

OSTEOMYELITIS

Acute pyogenic inflammation involves all the constituents of a bone, although it may be in different degree. It is a mistake to consider periostitis and osteomyelitis as separate diseases.

Etiology.—The *predisposing* causes are age, sex, and trauma. The great majority of acute infections occur during the period of

Fig. 285.—Acute infectious osteomyelitis. Vertical section through the lower leg and foot. Marrow of the shaft of the tibia almost entirely infiltrated with greenish-yellow purulent exudate. In places adjacent to the purulent exudate are areas of injected marrow. The exudate has extended through the lower epiphyseal line into the epiphysis. The thickening of the cortex of the shaft is due to a deposit of periosteal bone. The upper epiphyseal line has been perforated, and the epiphysis is infiltrated with purulent exudate. (E. H. Nichols in Keen's Surgery.)

active growth. The disease is three times as common in boys as in girls, probably because the former are more exposed to trauma. A history of some form of trauma, a blow or a strain, is often obtained. When a wrench is applied to a growing bone the part most likely to give way is the metaphysis, in which an effusion of blood may occur offering a suitable nidus to any waiting bacteria.

The *exciting* cause is one of the pyogenic organisms, usually the staphylococcus aureus, less frequently the staphylococcus albus, and

occasionally the streptococcus, the pneumococcus, and the typhoid bacillus, the last deserving a separate paragraph to itself. The infecting organism is carried to the bone by the blood stream. It enters the circulation from one of the usual septic foci in the body, of which the mouth and tonsils are probably the most important. Occasion-

Fig. 286.—Osteomyelitis of femur and tibia, showing sequestrum, cloacæ, and new bone formation.

ally suppuration of the skin, boils, infected wounds, or compound fractures may act as the source of infection. Suppuration may spread to the mastoid process from the middle ear.

The long bones are most frequently affected, particularly the upper and lower end of the tibia, the lower end of the femur, and the

upper end of the humerus. Almost any bone may occasionally be involved, even the vertebræ.

The point at which inflammation commences depends on the age of the patient. As my colleague Dr. A. Gibson points out, it is convenient for many purposes to distinguish two types of the disease, the juvenile and the adult. In the former the bone is still growing, and the epiphyses are still present. In the latter the development of the skeleton is complete. In the juvenile group the process almost

Fig. 287.—Marked new bone formation following osteomyelitis.

invariably commences in the metaphysis. The reasons for this predilection are two-fold: (1) this region possesses a peculiarly rich blood supply, and the vessels present the hair-pin bends already described; (2) it is this region which suffers most in twisting injuries to the joint. In the adult group the lesion may commence in any part of the bone. The liability of the metaphysis to infection in the young is strikingly

exemplified in a case recorded by Gibson. A boy, aged 12, developed evidence of acute inflammation in the left clavicular area, but nothing was found at operation. The autopsy revealed a small abscess at the root of the coracoid process of the scapula. The coracoid process is an epiphysis which remains separate until the fifteenth year.

The juvenile differs from the adult form in other respects. The juvenile cases are sometimes fulminating, ending fatally within 24 hours. The adult cases are never so acute. The juvenile cases always commence as an osteomyelitis; any periostitis is secondary. In the adult cases a primary osteomyelitis may occur.

Spread.—From the initial lesion the infection may spread rapidly down the medullary cavity till the greater part or the whole of the shaft may be involved. Spread to the periosteum also occurs readily, and that membrane becomes lifted off the bone.

Although this is the usually accepted teaching, reference must be made here to the work of Clarence Starr of Toronto. According to Starr acute hematogenous osteomyelitis is almost confined to children in whom the epiphysis is not yet fused with the diaphysis. It is commonest between the ages of two and ten. Osteomyelitis in the adult is due to direct injury to bone with primary infection, such as is found in compound fractures and bullet wounds. From a study of clinical material and of experimental osteomyelitis in dogs Starr arrives at the following conclusions. The infection commences in the metaphysis, and extends most easily along the epiphyseal line to the cortex and the periosteum. The pus formed under the periosteum strips it from the bone at an early stage, and proceeds to make its way along the shaft between the periosteum and the bone. As the result of the increased tension the pus probably spreads backward through the Haversian canals at different levels and invades the medulla from the cortex, giving a "spotty" character to the shaft infection. Thus instead of the periosteum covering the shaft being infected from the medulla, it is the medulla which is infected from the periosteum. Direct spread into the medulla from the original focus in the metaphysis is not an early occurrence, owing partly to the distance which separates the two in the case of a long bone. This intervening tissue was found free from bacteria in the human cases which were examined bacteriologically. The firm attachment of the periosteum to the epiphyseal line in the child prevents the spread of the pus into the joint.

Morbid Anatomy.—The process is a suppurative one, the medulla becomes converted into an oily pus owing to destruction of the fatty tissue, and the surface of the bone is bathed in pus which also fills the Haversian canals. At first the surface, from which the periosteum is raised, presents the usual healthy shining appearance, but soon it becomes of a dull opaque white, and at a later date, when a sequestrium has formed, it may be of a dark brown color; the surface is usually rough and pitted owing to the erosive action of the granulations lining the deep surface of the new case. As long as the surface is

separated from the periosteum by a layer of pus it remains smooth. Thrombosis of the veins is constant, and in addition to still further interfering with the supply of nourishment to the part, the septic thrombi thus formed may occasionally give rise to emboli and general pyemia, of which ulcerative endocarditis may be a feature and may still further increase the gravity of the condition.

The adjacent joint may become filled with a sterile serous effusion, or the bacteria may occasionally invade the joint and set up a purulent inflammation.

Fig. 288.—Acute osteomyelitis with sequestrum formation.

A greater or less extent of the bone dies, and in the course of a month or two a sequestrum is formed. The periosteum rapidly lays down a *new case* which in time may take the place of the dead bone. It is perforated here and there by *cloacæ*, through which pus from the dead bone continues to discharge. There is a rare variety of sequestrum formation in which the medullary cavity is lined by a thin tube

of dead densely hard bone, which may be readily separated from the living bone of the shaft. In such a case it would almost seem as if there had been a primary infection of the medulla of the bone.

Bones developed in membrane, as the flat bones of the skull and the upper jaw, are not reproduced to any extent. Where the peri-

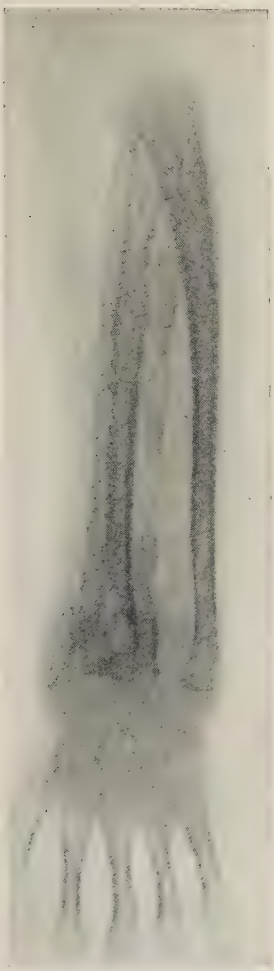

FIG. 289.—Acute osteomyelitis. Involucrum well shown.

FIG. 290.—Osteomyelitis of the tibia with marked proliferative changes.

osteum has been completely destroyed no new bone is formed, so that the new case may be of a patchy character.

Chronic Osteomyelitis.—When a bone has once been infected, the bacteria may lurk in its depths for months or years, giving rise to recurring attacks. This relapsing form of osteomyelitis is especially common in adults.

A chronic circumscribed abscess, called a *Brodie's abscess*, may form in one of the ends of a long bone, it may be years after the original infection. The common site is the upper end of the tibia, but the lower

Fig. 291.—Extensive acute periostitis involving nearly the entire shaft. The cortex is intact.

Fig. 292.—Chronic abscess of lower end of tibia rupturing into ankle joint. A rod passes through the perforation which was much smaller in the fresh specimen.

end of the femur, the upper end of the humerus, and other parts, may also be affected. During periods of quiescence there is a small cavity containing clear, serous, sterile fluid, and surrounded by a zone of

densely sclerosed bone, casting a deep shadow in the X-ray picture, but when the process becomes active the cavity becomes filled with greenish-yellow pus from which the staphylococcus can be isolated, and it is lined by a layer of granulation tissue.

Typhoid Osteomyelitis.—Mention has already been made of the typhoid bacillus as a cause of osteomyelitis. The bone marrow may readily be infected in such a septicemic condition as typhoid fever, but the bacilli rarely succeed in establishing themselves. When symptoms appear it is usually about the end of the second month, but there is no form of bone disease in which the infection may be more latent, and it may be many years before signs of inflammation manifest themselves. The bacilli have been obtained in pure culture as many as 20 years after the original infection. The bones usually involved are the upper end of the tibia, the ribs and the sternum.

The pathological lesion is somewhat variable, but usually consists of a collection of greenish or brownish pus under the periosteum, in the metaphysis, or in the shaft. The condition may be subacute or chronic. Sequestrum formation is rare, for the process is rather one of molecular death than death en masse, of caries rather than necrosis.

TUBERCULOSIS OF BONE

There is a tendency to regard tuberculosis of bone as a peculiar disease, something apart from the manifestations of tuberculosis elsewhere, and the use of a number of special descriptive names for types and for marked appearances has confirmed this impression. The disease, however, merely follows the general lines already described in the chapter on tuberculosis, with certain modifications necessary because of the anatomical peculiarities of the part.

Bone tuberculosis is a chronic inflammatory condition, an osteomyelitis with secondary periosteal involvement, occurring in early life, choosing particularly the ends of the long bones, the short long bones, and the short bones, displaying as a rule an excess of bone destruction over bone formation, and yet with a decided tendency towards limitation of spread and spontaneous healing owing to the fibrous tissue formation so characteristic of tuberculous disease in the lungs and other organs.

Site of Infection.—The infection is carried to the bone by the blood stream, probably in the form of a tuberculous embolus, from some other focus in the body. Tuberculosis commences in cancellous bone, seldom in compact bone, and the most frequent victims are the ends of the long bones, especially the tibia and femur, the short long bones, the short bones of the carpus and tarsus, and the vertebræ. As all of these are in close proximity to joints, bone and joint tuberculosis are very frequently associated.

The first part to be affected is usually the metaphysis or epiphysis of a long bone. Both of these are richly supplied with capillary loops in which an infected embolus may readily lodge. The circulus vasculosus, containing the vessels responsible for carrying the infection, lies in

the reflexion of the synovial membrane on to the bone. When the reflexion includes the metaphysis, as at the upper end of the femur, the disease will originate in that part. When, on the other hand, the reflexion lies entirely in relation to the epiphysis, as at the upper end of the humerus, and, to a lesser extent, at the lower end of the femur, the primary focus will be in the epiphysis.

There is a further factor which may well determine which bone is to be attacked. In tuberculosis, say of the lungs, there is frequently an obliterating endarteritis of the vessels in the marrow due to the circulating tuberculous toxins, which diminishes the blood supply, gives rise to a cell sickness, and so predisposes the part to invasion by the tubercle bacillus. This endarteritis is irregular in its distribution, thus resembling arteriosclerosis, and one bone may be taken while another is left.

Fig. 293.—Tuberculosis of head of femur; the articular cartilage has been stripped off.

The Primary Bone Lesion.—The bacilli reach the marrow of the cancellous bone in a metaphysis or epiphysis by one of two routes. (1) An intravascular route, in which the bacilli are carried by the blood stream into the center of the bone; (2) a perivascular route, in which the infection commences in the synovial membrane of the joint, and spreads slowly along the perivascular lymphatics to the interior of the bone.

A miliary tubercle is formed composed of a central mass of endothelial cells and a surrounding zone of lymphocytes. It appears as a small grey point. As fresh tubercles are formed and the disease spreads, characteristic changes occur in all the constituents of the bone, and these may now be briefly considered.

The *marrow* around the focus shows the tissue changes one is accustomed to associate with tuberculosis in the lungs and elsewhere. For the first week the response is that to an acute irritant, and a leucoblastic reaction on the part of the marrow gives rise to great numbers

of polymorphonuclears. The tuberculous toxins then begin to make their presence felt, and the lymphocyte replaces the polymorph. Later still the fibrosis which plays so important a part in the limitation of tuberculosis begins to develop, the fat is replaced by connective tissue, and in time the original focus becomes walled off by a dense zone of fibrous tissue, which is yellowish-white in color and remarkably firm to the touch. Invasion of the focus by the fibrous tissue may eventually bring about complete cure. In the acute spreading form there is little or no fibrosis. The arteries of the marrow and also of the bone itself frequently show an extremely marked condition of endarteritis obliterans, similar to that so characteristic of syphilis

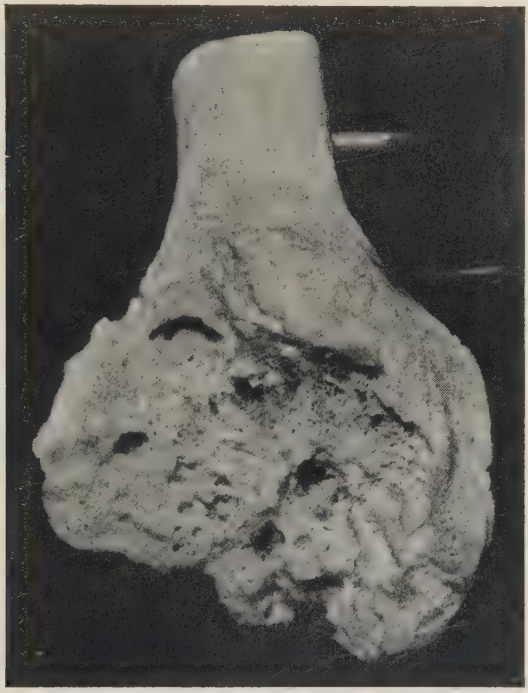

FIG. 294.—Tuberculosis of lower end of tibia.

save that it is unaccompanied by a perivascular infiltration of lymphocytes. The relation of this arterial change to the toxins of the disease has already been discussed.

The *bone lamellæ* show two characteristic changes, osteoporosis or rarefaction and osteosclerosis or condensation. These merely correspond to tissue destruction and fibrosis in tuberculosis elsewhere. *Osteoporosis* or caries is brought about by two agencies: (1) the action of osteoclasts, and (2) the erosive influence of a cellular granulation tissue which is formed in relation to the blood vessels, and which enlarges the Haversian canals and erodes the bone under the perios-

teum and in contact with the medulla. Branching trabeculæ of bone are left, the interspaces being filled with granulation tissue. *Osteosclerosis*, which is seldom marked in tuberculosis, being much more characteristic of syphilis, is the analogous process in the bone to fibrosis in the marrow. Through the action of osteoblasts fresh layers of bone are deposited on the surface of the laminæ, so as to increase their thickness and consequently the denseness of the bone.

The *periosteum* is early stimulated to activity, owing to the increased vascularity, the result of the underlying bone disease. The character of the new bone formed is peculiar; it is usually quite can-

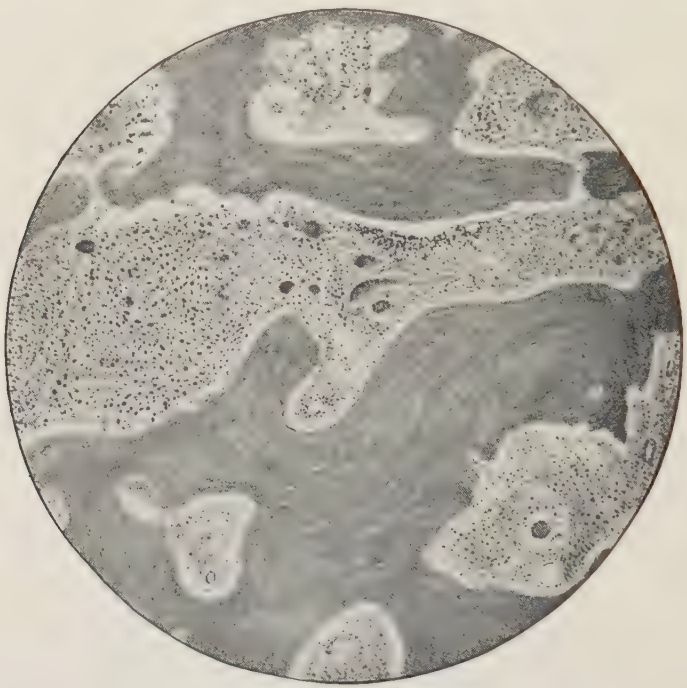

Fig. 295.—Tuberculous osteitis. The bone is becoming rarefied by the formation of tuberculous granulation tissue in which numerous giant cells can be seen.

cellous, and only compact close to a joint where movement would be interfered with by the more abundant porous bone. If new bone were deposited directly on the smooth surface of the shaft it would be but poorly attached and would readily be broken off. The osteoclasts, therefore, which are found on the deep surface of the periosteum, first excavate a series of holes along the shaft, until the smooth surface has become quite rough. The osteoblasts now deposit bone upon the roughened surface. This new bone is not laid down uniformly but in the form of arches, between which there is a small quantity of granulation tissue. A series of tiers of arches is thus formed, an

architectural device by means of which a maximum of strength with a minimum of weight is obtained.

Progress of the Disease.—Tuberculosis may behave in various ways in bone as in other organs. It is unnecessary, however, to introduce a special series of names to denote the different varieties. It will be sufficient if we recognize a localized form and a spreading form, with a third variety which deserves special consideration, the atrophic form or caries sicca.

The *localized form* is much the commoner. The defence is sufficiently strong to hold the disease in check. It corresponds to a localized nodule in the lung. The lesion, usually about the size of a marble, presents a center which is either caseous or converted into a semi-fluid material. Around this there is a pale pink zone, blending with the surrounding marrow. This is the limiting band of new fibrous tissue. The condition is essentially chronic, so that the slow process of rarefaction or caries, due to the activity of osteoclasts and granulation tissue, usually results in complete absorption of the lamellæ. If, however, separation of the lamellæ occurs before absorption is complete, they become necrosed and form small sequestra.

Fig. 296.—Tuberculosis of femur. Destructive process involving the inner part of the lower epiphysis.

The *spreading form* may be described as a tuberculous osteomyelitis in which the fibrosis is insufficient to limit the spread of the disease. It corresponds to a diffuse tuberculosis of the lung. The central caseous mass is surrounded by a zone of grey infiltration, representing tuberculous granulation tissue which has not yet become caseous. Around this again there is a red zone of reaction. Thrombosis of the vessels occurs at an early stage and greatly weakens the resisting power. Rarefaction is not a marked feature, for before it has time to proceed far necrosis supervenes, active processes are arrested, and comparatively large sequestra are formed. The periosteum, as usual, displays marked activity, and lays down an abundant supply of new bone.

The disease may spread down the medullary cavity, until the greater part or the whole of the shaft is involved. It may spread through the epiphyseal cartilage, involving the epiphysis and the adjacent joint. It may spread to the periosteum, where it forms a subperiostial cold abscess, and may then involve the soft parts, giving rise to a cold abscess which may ultimately discharge on the skin.

Where the medullary spread is a marked feature the shaft of the bone may become much swollen and expanded, owing to absorption of the interior of the bone by granulation tissue and deposition of new bone on the surface by the periosteum. This is best seen in *tuberculous dactylitis*, in which a metacarpal bone or more commonly a phalanx presents a spindle-shaped swelling, which must be differentiated from the similar swelling produced by congenital syphilis.

Caries Sicca.—This a rare condition, chiefly affecting the upper end of the humerus. The deeper portion of the bone becomes rarefied owing to the formation of granulation tissue, and new bone is deposited

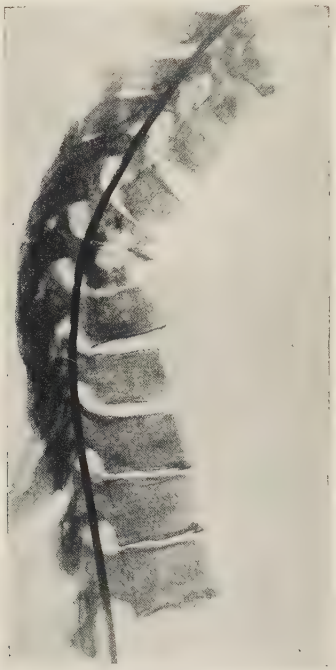

Fig. 297.—X-ray picture of tuberculosis of the spine (central form). There is marked destruction and collapse of the bodies of the vertebræ.

on the surface, which itself, however, becomes in turn eroded. Finally the granulation tissue become dried up and fibrosed. True suppuration never occurs.

Tuberculosis of the Vertebræ.—The vertebræ are more frequently affected by tuberculosis than any other bones in the body. The disease is commonest in children, particularly during the first 5 years of life. The interior of the body of a vertebra is supplied with blood by a branch from the posterior spinal artery which enters the posterior surface of the bone. A limited area of the front of the body is supplied by branches from the intercostal arteries.

There are two main forms of the disease, the central and the peripheral. The *central form*, which is very much the commoner, begins in the center of the body, which gradually becomes hollowed out until it is no longer able to support the weight of the vertebræ above

Fig. 298.—Tuberculosis of spine; extensive periosteal involvement; no deformity.

and collapses, giving rise to an angular deformity. One or more vertebræ may be involved. The *peripheral form* affects that portion of the anterior surface which is supplied from the intercostal vessels.

It is only found in adults, and as it leaves the greater part of the body of the vertebra intact it causes little or no deformity.

The paralysis which may complicate the later stages of the disease is not due to the angular deformity of the spine, but to an edema of the meninges, or to the cold abscess which forms under the posterior common ligament, and, gradually passing backwards, comes to press upon the spinal cord.

Fig. 299.—Syphilitic periostitis and osteophyte formation. (MacCallum.)

The pus may trek in almost any direction. It may pass along a rib under the periosteum and appear at a considerable distance from the original focus, so that in every case of tuberculosis of a rib the spine should be carefully examined. Or it may pass down within the sheath of the psoas muscle and appear as a psoas abscess under Poupart's ligament.

In the *skull* the disease usually commences in the diploe, and extends outwards so as to perforate the outer table. See page 631.

SYPHILIS OF BONE

As syphilis in the early stages is a septicemia, and as the bones are the chief hemopoietic organs in the body, we should expect that bony involvement in syphilis would be common. It is impossible to make any exact statement regarding the frequency of syphilis of bone. Judged by obvious gross changes such as tumefaction it is much rarer than tuberculosis. On the other hand in the early stages frequent symptoms, such as the nocturnal bone pains, are probably due to definite bony involvement, although no obvious anatomical lesion may be demonstrable. Further, it must be remembered that the recent researches of Warthin have shown that the common lesion in syphilis is not the gumma, although it is that which obtrudes itself on the notice of the surgeon, that much more frequently a widespread dissemination of the spirochetes gives rise to a diffuse syphilitic infiltration which later becomes a fibrosis, and that such a condition as the so-called hypertrophic form of bone tuberculosis is much more probably really syphilitic in nature.

Syphilis of bone differs from tuberculosis in that it affects different parts—the diaphysis of long bones rather than the articular ends—involvement of joints very seldom occurs, and sclerosis is much more prominent than rarefaction, whereas in tuberculosis the reverse is the case. Patients with syphilis of the bones seldom develop neurological manifestations, a fact which supports the view that there are

different strains of spirochetes, some with an affinity for ectodermal, others for mesodermal structures.

The bones may be affected either in acquired or in congenital syphilis. The acquired form will first be described, and the lesions peculiar to the congenital variety considered later. The fundamental pathology of both forms is identical.

The bones most commonly involved are the tibia, the sternum, the skull, and the bones of the face. Recent work has shown that the vertebral column, especially the cervical portion, is much more frequently involved than used to be supposed. Although it is improbable that the spirochetes are entirely limited to one part of the bone, the brunt of the attack may fall on the periosteum or on the marrow

Fig. 300.—Extensive syphilitic necrosis of the calvarium. (Specimen in the Warren Museum of the Harvard Medical School.)

in the medulla, so that we may speak of a periosteal and an endosteal form of the disease. The periosteal variety, at least in its clinical manifestations, is much the more common.

Periosteal Form.—The spirochetes settle particularly in the vascular tissue of the deeper layers of the periosteum. The tibia may be taken as a typical example. The usual perivascular infiltration of round cells occurs, and soon an abundant highly cellular granulation tissue is formed around the vessels, not merely in the periosteum but also in the Haversian canals. A transient periostitis associated with

nocturnal boring pains is common in the early secondary stage of the disease, affecting particularly the tibia and the frontal bone.

Later in the disease the process is more persistent. The new granulation tissue erodes the surface of the bone and widens the Haversian canals, giving the bone a highly characteristic worm-eaten appearance, best seen in the case of the skull. The presence of the spirochetes, however, stimulates the osteoblasts to great activity, and an abundant formation of new bone is laid down: (1) on the surface, where

Fig. 301.—Syphilitic condensation and thickening of the tibia.

the process may be uniform or where osteophytes suggestive but not pathognomonic of syphilis may be formed, and (2) on the walls of the dilated Haversian canals, so that the shaft of the bone may become extremely dense and heavy, with obliteration of the medullary cavity. The thickening may be localized so as to form a fusiform node, or may be diffuse and involve the greater part of the shaft. This periosteal

reaction is usually absent in the skull and other bones which develop in membrane.

Still later interference with the blood supply due to an obliterating endarteritis may lead to degenerative changes in the center of the mass, and a typical gumma is formed. The central part undergoes caseation and softening, and the skin may become involved with the formation of a typical syphilitic ulcer.

The blood supply may be cut off so rapidly that a portion of the bone dies and a sequestrum is formed, which separates but slowly and

FIG. 302.—Normal epiphyseal line. (De Lee.)

incompletely from the surrounding bone owing to the comparative inactivity of the rarefaction process. Such a sequestrum is usually very dense and heavy. Considerable areas in the skull, nasal bones, nasal septum, and hard palate may be destroyed in this way, although these late results are seldom seen with modern methods of treatment.

Endosteal Form.—Gummata, gelatinous in appearance and often of a bright yellow color owing to the high fat content, may be formed in the bone marrow. These when small may give rise to no external

manifestations. Sometimes, however, and this is particularly the case in the phalanges in congenital syphilis, there may be a diffuse infiltration of the entire marrow with erosion and expansion of the interior of the bone and a corresponding formation of new periosteal bone on the surface. The result is a spindle-shaped swelling, a syphilitic dactylitis, closely resembling in outward appearance the similar con-

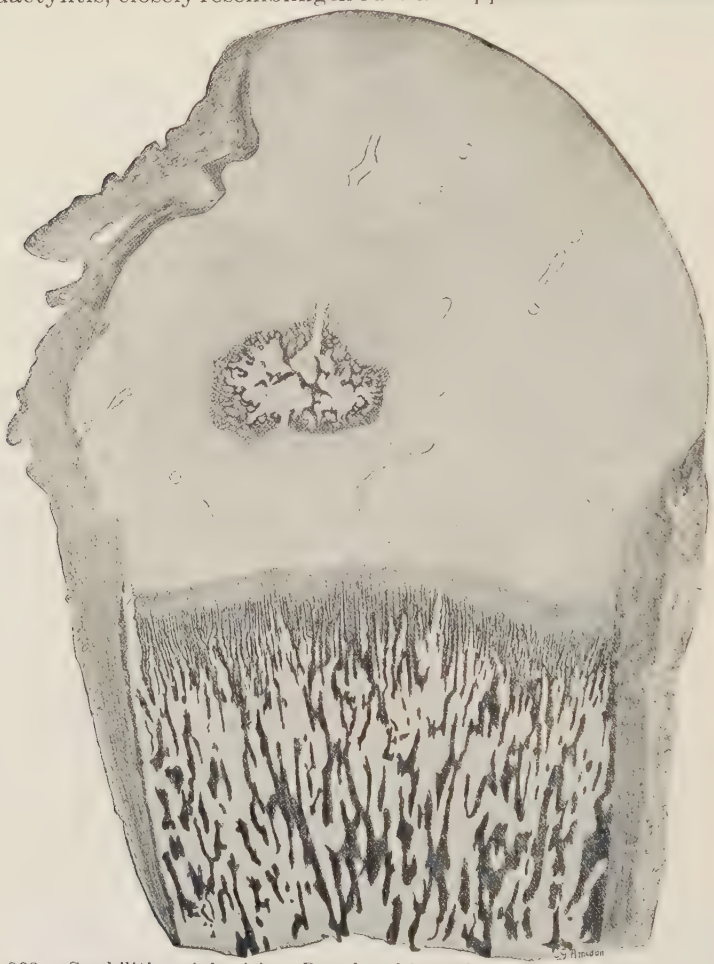

FIG. 303.—Syphilitic epiphysitis. Broad and irregular epiphyseal line. (De Lee.)

dition found in tuberculosis. The shaft of a long bone may be so weakened by this endosteal expansion that a pathological fracture may result. In the rare cases where the articular end of the bone is affected the joint may become involved, with the production of syphilitic arthritis.

The *vertebræ* may be the seat of a syphilitic periostitis or of gummatous formation in the center of the body. Rarefaction rather than

Syphilitic epiphysitis. Note the characteristic yellow line. Gross specimen furnished by Professor F. Robert Zeit (DeLee).

caseation is the rule, so that the kyphosis so frequently seen in Pott's disease is less commonly observed in syphilitic disease. As a rule only one vertebra is involved, another point which may serve to differentiate it from tuberculosis. In any case of apparent Pott's disease in an adult it is well to do a Wassermann test.

Congenital Syphilis.—The bones are more commonly involved in congenital than in acquired syphilis. The lesions of infancy differ from those which develop later in childhood and will be considered separately.

In infancy the important lesions are (1) epiphysitis, (2) bossing of the skull, and (3) craniotabes.

Syphilitic epiphysitis is a very constant and characteristic lesion in the new-bone, particularly affecting the bones about the knee. The normal, thin, pearly-grey line of the epiphyseal cartilage becomes broad, irregular, opaque, yellowish-white, and may be granular and gritty in appearance. The place of the epiphyseal cartilage is taken by syphilitic granulation tissue which invades the neighboring young bone, so that when necrosis and caseation occur a mass of minute bony particles results, giving an appearance not unlike that of mortar.

The epiphyseal line instead of forming a union between the epiphysis and diaphysis now becomes a space separating the two, so that growth in length ceases and the infant is unable to use the limb, so that it appears to be paralyzed. Indeed the name syphilitic pseudo-paralysis has been applied to the condition. Under appropriate treatment, however, firm union will take place and growth in length will again commence.

Bossing of the skull is due to a subperiosteal formation of new spongy bone giving rise to bosses known as Parrot's nodes. These are usually arranged around the anterior fontanelle, giving the so-called "hot-cross bun" appearance. Early treatment results in the disappearance of the bosses, but if the bone becomes sclerosed the condition is permanent.

Craniotabes is a condition of softening and rarefaction, in which the bone appears to revert to its original membranous state, and may become as thin as parchment. It affects the posterior part of the skull, the occipital and parietal bones. The condition responds well to treatment.

In older children the lesions resemble rather those of the acquired form, and are gummatous in nature.

The *tibia* may be markedly thickened, or it may be compressed laterally and curved forwards, giving the "sabre-blade" deformity.

The *phalanges* may show the combination of endosteal and periosteal involvement already described as syphilitic dactylitis.

The *nose* and the *palate* are frequently the seat of gummatous formation with resulting destruction, sometimes of a very extensive nature, so that the bridge of the nose may fall in (saddle-nose), and a large perforation of the palate may appear.

TUMORS OF BONE

The common tumors affecting bone are osteoma, chondroma, sarcoma, and secondary carcinoma. These will first be considered, and passing reference will then be made to the numerous other rare forms which may occur.

Osteoma.—It is singularly difficult to know what exactly should be included in the group of osteomata. The difficulty is to determine whether a new formation of bone should or should not be regarded as a true neoplasm. So many inflammatory and traumatic conditions may be associated with bony formation. The callus following a fracture, the new formation in osteomyelitis and syphilis, the ossification of inflammatory exudates in various parts of the body, the condition known as myositis ossificans, the bony outgrowths around joints the seat of chronic arthritis, do not present any essential differences from the masses of bone which are recognized as true osteomas. The histological picture is of little value as a means of differentiation. The gross appearance and the clinical features are the factors most worthy of consideration.

Osteomata usually arise from the surface of the bone; they are then called exostoses. When they arise in the center of the bone they are known as enostoses; these usually occur in the diploe of the skull and the bones of the face.

An osteoma arising from compact bone forms a *compact osteoma*, one arising from cancellous bone forms a *cancellous osteoma*. The former are derived directly from the periosteum and are most frequently found on the skull. The latter are derived from cartilage, and occur chiefly at the articular ends of the long bones.

The largest group of exostoses are those which originate at the ends of the long bones, and which are peculiar in being multiple, frequently hereditary, and often associated with abnormalities of growth. As the condition is rather one of disturbance in the process of ossification than a neoplastic process it is considered on page 740 as hereditary deforming chondrodysplasia. Other small exostoses are frequently traumatic in origin, the blow appearing to cause a displacement of cells which then take on an abnormal growth.

The *subungual exostosis* is a variety of osteoma which arises from the dorsal aspect of the terminal phalanx of the big toe. Although it does not attain to any great size it causes great pain and disability as it lifts up the nail and may erode the matrix and the soft parts. It differs from ordinary exostoses in that it forms adhesions with surrounding tissues.

The face is a not infrequent site of osteoma. The tumor may grow into the orbit, displacing the eye, or it may invade the various sinuses or the antrum of Highmore. In the peculiar and fortunately rare condition of diffuse osteoma or leontiasis ossea there is a diffuse overgrowth of the bones of the face. commencing in the upper jaws, and producing terrible deformity.

Chondroma.—Cartilaginous tumors of the bone occur during the growing period, and tend to cease growth when that period is over. Although occurring in bone they arise for the most part from portions of cartilage which have probably become misplaced through some error of development.

The short bones of the hands and feet are common sites of chondroma, but the tumor may occur at the ends of the long bones, the pelvis, ribs, and scapula, rarely in the skull.

Chondromata usually grow from the surface of a bone. When they arise in the interior of the bone they are known as enchondromas. Occasionally a chondroma will attain an enormous size. I have seen a cartilaginous tumor of the sternum which occupied so large a portion of the thoracic cavity that when it was removed the patient died of acute dilatation of the heart. Chondromas of the pelvis may form a most serious complication during pregnancy and parturition.

A characteristic feature is the lobulation of the surface. This is due to expansive growth from multiple centers. The tumor is, as a rule, well encapsulated and can be readily shelled out. Occasionally, however, it may encroach on surrounding tissues, and in some cases the tumor shows a curious tendency to invade the veins, travelling for a long distance along them.

Degenerative changes are frequent. The hyaline cartilage may undergo myxomatous degeneration, so that cyst-like cavities are formed containing a glairy, mucinous material. Calcification and ossification are of frequent occurrence, especially in chondromata which have ceased to grow. The change can readily be detected in X-ray pictures.

Sarcomatous degeneration is the most important change to which chondromata are liable. It is always open to debate, however, whether the tumor was not malignant from the beginning. Although the invasion of veins already referred to is most common in frank chondrosarcomas, yet it may occur in tumors which display no histological evidence of malignancy. In the chondrosarcoma the regular arrangement of cartilage cells is lost, at least in parts of the tumor, and the growth is much softer and more cellular in character. Invasion of the veins is followed by distant metastases, notably in the lungs.

The condition of multiple chondromata or multiple cartilaginous exostoses, not being an example of true tumor growth, is described on page 740.

Sarcoma.—Sarcomata are the commonest of bone tumors. They occur most frequently in childhood and early adult life. They include amongst their members some of the most malignant and rapidly fatal of all tumors. On the other hand some are of so comparatively benign a character that one hesitates to include them in the group of sarcomata.

Malignant connective tissue tumors of bone may arise either from bone cells (osteogenic tumors) or from the cells of bone-marrow. The former alone are considered as true sarcomata.

The factors which predicpose towards the development of an osteogenic sarcoma are not understood. The tumors are commoner in young subjects. They almost always begin at the end of the diaphysis, that is to say in that part of the bone which is specially well supplied with blood and which we have already seen is the usual site of bacterial infections. If trauma or irritation plays any part it is only when it has the opportunity to act for a long time in a chronic form. Although exuberant callus so closely resembles osteogenic sarcoma in structure there appears to be absolutely no relation between fracture and sarcoma.

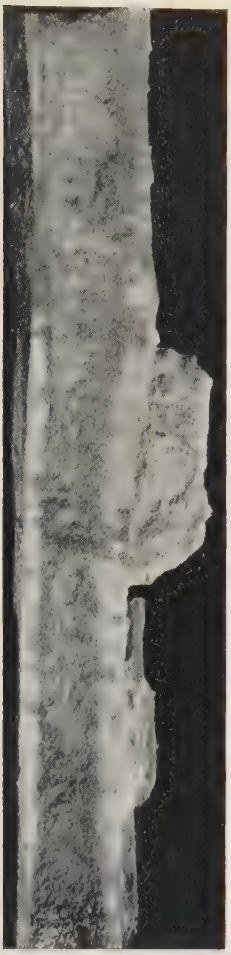

Fig. 304.—Periosteal sarcoma of the tibia. The cortex of the bone is quite intact.

The osteogenic sarcomata arising from osteoblasts have been divided by Ewing into four main groups. This subdivision is by no means unnecessary, for the groups differ not only in structure, but also in their X-ray appearance, their clinical behavior, and their response to treatment. The four groups are: (1) periosteal sarcoma, (2) subperiosteal and medullary sarcoma, (3) telangiectatic sarcoma, and (4) sclerosing osteogenic sarcoma.

1. *Periosteal Sarcoma.*—Not only is this type of tumor periosteal, it is extraperiosteal, in distinction to the second group of subperiosteal growths. Occurring as a rule at the ends of such long bones as the femur, tibia, and humerus, it may develop in almost any bone of the body. The bone shaft remains intact or is but slightly eroded, whereas in the subperiosteal variety it is extensively involved. This intact character is beautifully shown in X-ray pictures, where the shaft can be seen running through the tumor mass. A periosteal sarcoma usually remains encapsulated for a long time, pushing the soft parts in front of it.

Bone formation in different degrees of completeness may be found, and occasionally this is so marked that the term *ossifying sarcoma* may be used. In such cases numerous spicules or needles of new bone are found penetrating the tumor, sometimes in a fan-like fashion. In an ossifying sarcoma of the skull which I studied the entire mass was pervaded with spines and stalactites like "huge teeth of splintered crystal." When such a growth invades the neighboring muscles the result may be a condition resembling myositis ossificans.

Microscopically two main types of growth must be distinguished. The first is a fibrosarcoma composed of rather large spindle cells with

a great amount of hyaline, fibrous, or osseous stroma, which imparts to the tumor a characteristic firmness. This is perhaps the most favorable type of bone sarcoma for amputation. In the second form the tumor is much more cellular, the cells being small and spindle-shaped with hyperchromatic nuclei. Such tumors are soft, crumbly, and extremely malignant.

2. *Subperiosteal and Medullary Sarcoma.*—In this, the commonest of the osteogenic sarcomas, the tumor involves all three of the main

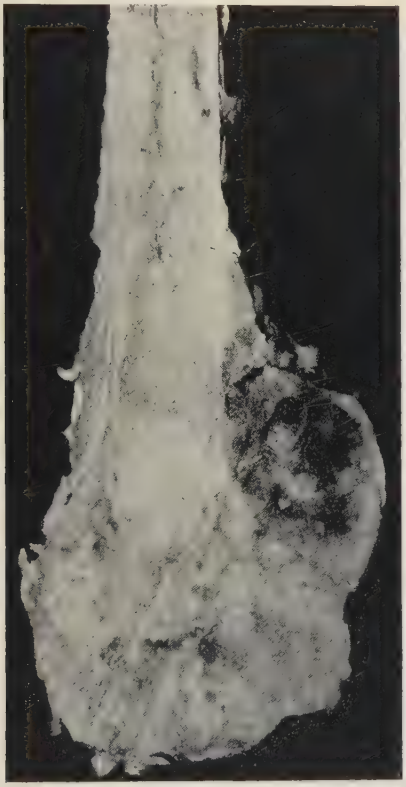

FIG. 305.—Sarcoma of lower end of femur involving both medulla and periosteum. An example of the subperiosteal and medullary form.

FIG. 306.—Sarcoma of humerus with complete destruction of bone. Subperiosteal and medullary form.

portions of the bone—the marrow, the shaft, and the subperiosteal tissue. The medullary cavity is filled by the tumor, the shaft is destroyed, and the periosteum is lifted from the surface of the bone. An elongated swelling is the result which has been likened to a leg of mutton. Perforation of the periosteum is followed by invasion of the soft parts. The X-ray picture is characteristic, for the periosteum is seen to be raised, the cortex destroyed, and the bony capsule of the giant-cell tumor is completely absent.

Microscopically the tumor is made up of round or spindle cells with hyperchromatic nuclei. There may be some new bone formation, but there is quite as much bone destruction, and for that reason foreign body giant cells may be seen. In addition there may be true tumor giant cells, and mononuclear giant cells are common.

3. *Telangiectatic Sarcoma.*—In this variety there is a great development of blood vessels in the midst of a soft mass of cellular tissue. The tumor involves the medulla, the shaft, and the periosteum, and its exact starting point is not a matter of certainty. It is rapidly

FIG. 307.—Telangiectatic sarcoma of the femur. The tumor was so vascular that blood dripped profusely from the cut surface.

destructive, causes expansion of the shaft with the familiar phenomenon of egg-shell crackling, leads to spontaneous fracture at a comparatively early date, and seldom displays a marked tendency to ossification. It is one of the most malignant of bone sarcomas, and no cures have been recorded.

The condition known as a *malignant bone aneurism,* in which marked pulsation is observed in the tumor mass, is one manifestation of the growth under consideration. True pulsation is never found in a periosteal sarcoma.

A telangiectatic sarcoma may bear a close resemblance to the benign giant-cell tumor of bone, as the latter growth may be extremely vascular, and, although bone destruction is usually very much more advanced in the former than in the latter, a microscopic examination may be necessary before a correct diagnosis can be made.

4. *Sclerosing Sarcoma.*—Although somewhat dense formations of bone may occur in many sarcomas, there is one variety in which the sclerosing process is so pronounced and widespread that it deserves special consideration, especially as the clinical features are somewhat distinctive.

The medullary cavity at one end of a long bone becomes filled and obliterated by a dense mass of compact bone, which gives a radio-

FIG. 308.—Telangiectatic sarcoma of femur with pathological fracture.

logical picture unlike that of any other bone disease. The tumor consists of the usual spindle and polygonal cells, but the essential feature is the great amount of dense intercellular osteoid tissue or actual bone.

Growth is very slow and there is rarely any invasion of the surrounding soft parts, but the character of the tumor cannot be saved by

these features, for metastases in distant organs occur sooner or later, although death may be delayed for ten or twenty years.

Endothelioma of Bone.—The recognition of this bone tumor is of importance, because in the past it has usually been mistaken for osteogenic sarcoma. It arises from the endothelium of the blood vessels or lymph vessels in the bone or the bone marrow. It occurs in two main forms: (1) angio-endothelioma, and (2) diffuse endothelioma.

Fig. 309.—Angio-endothelioma of humerus. (Ewing.)

The *angio-endothelioma* closely resembles the telangiectatic form of bone sarcoma, producing great bone destruction. The periosteum extending beyond the tumor mass is not involved as it is in osteogenic sarcoma. The tumor shows expansile pulsation, and constitutes one variety of bone aneurism. It usually occurs after the age of forty.

Microscopically it consists of sheets of clear endothelial cells surrounding large blood spaces.

The *diffuse endothelioma*, which is the more common form, occurs in young people, usually below the age of twenty. A large segment or the entire length of the shaft may be involved, this constituting the most striking characteristic of the growth. The shaft is slightly widened and destroyed, with no new bone formation. In the course of time metastases are set up. The tumor consists of sheets of very clear polyhedral cells, the dark nuclei of which may be mistaken for a round-cell sarcoma in poorly fixed tissue.

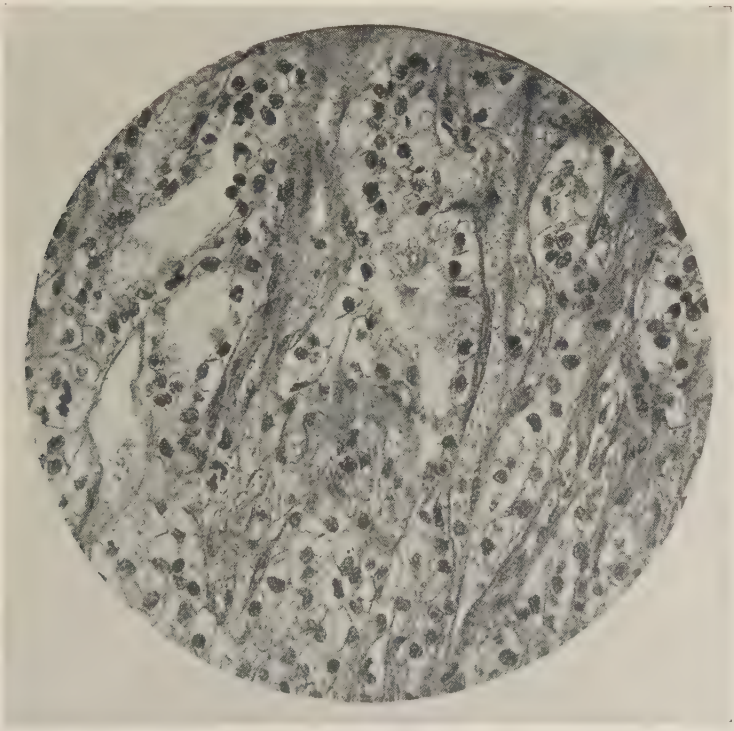

FIG. 310.—Structure of angio-endothelioma of bone. (Ewing.)

The tumor responds remarkably well to radiation by X-rays or radium. It must be remembered, however, that a myeloma, which is also centrally situated, responds equally well to radiation.

Giant-cell Tumor.—This condition is usually known by the name of giant-cell sarcoma. It is also called a myeloid sarcoma or myeloma. None of these names are satisfactory. It is certainly not a bone marrow tumor. Nor should it be called a sarcoma, for that term inevitably suggests malignancy, and this tumor, although locally destructive, probably never presents any of the general features of malignancy. As the result, however, of repeated local irritation in the form of

curettage it has been known to develop into a malignant spindle-cell sarcoma. Barrie considers that the process is inflammatory and not neoplastic, and to him it is a chronic hemorrhagic osteomyelitis.

Giant-cell tumors are found in the maxillæ, the ends of the long bones, tendon sheaths, bursæ, and the capsule of joints. A very typical specimen which I use for teaching purposes was removed from the flexon tendon sheath of the index finger.

Fig. 311.—Diffuse endothelioma of radius. Diffuse absorption without destruction of shaft. Spontaneous fracture. Wide invasion of muscle. Duration one year. (Ewing.)

A distinct relationship appears to exist between giant-cell tumors and osteitis fibrosa cystica. Giant cells are frequently found in this condition, and quite often such a tumor will originate in the wall of one of the cysts. This may be used as an additional argument against the neoplastic nature of the condition.

A giant-cell tumor may be periosteal or medullary in type. The former occurs in the maxillæ, and constitutes the commonest form of epulis. It is usually of firm consistency and slow growth. It may cause great expansion of the bone, but it seldom attains a large size. In one case which I examined so thin a bony shell was left that there appeared to be immediate risk of fracture of the mandible.

The medullary type is found at the ends of the long bones, particularly the lower end of the femur and the upper end of the tibia. The gross appearance is characteristic, and must be carefully distinguished from that of a malignant telangiectatic sarcoma of bone, for

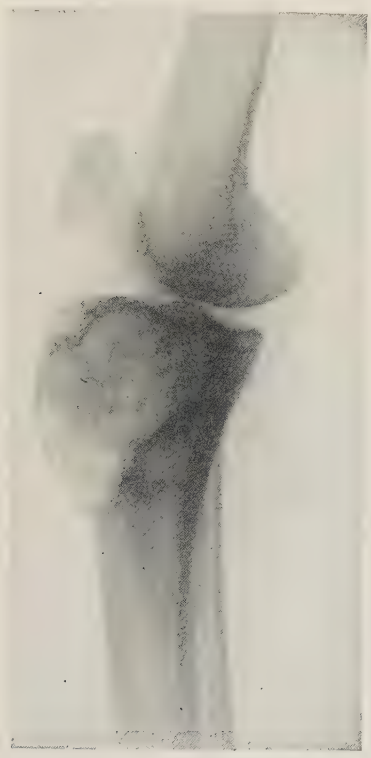

Fig. 312.—Giant-cell tumor of upper end of tibia. The multicystic appearance and the sharp limitation of the growth with complete absence of infiltration are well shown.

the treatment is essentially different. The tumor is very vascular, and recalls young granulation tissue. It is dark red in color, but white areas may be mixed with the dark, so that a mottled appearance results. In consistency it is soft, almost jelly-like, but it can be broken up into small pieces by the finger, although not into the finely granular masses characteristic of a highly cellular sarcoma.

Cyst formation may occur in the center, and the cyst is usually filled with blood. The cancellous tissue at the end of the bone is

absorbed until a mere shell remains, but this shell is continually reinforced by new formation from the periosteum. In this way great expansion may occur, but the rarefied nature of the mass is well seen in the X-ray picture, which shows a highly characteristic multicystic appearance with sharp limitation from the soft tissues.

Microscopically the tumor is made up of spindle-shaped cells without hyperchromatic nuclei, but in addition there are the characteristic giant cells which give the condition its name. These may be very numerous in one part of the mass, scanty or absent in another. The giant cells have the general characteristics of foreign body giant cells.

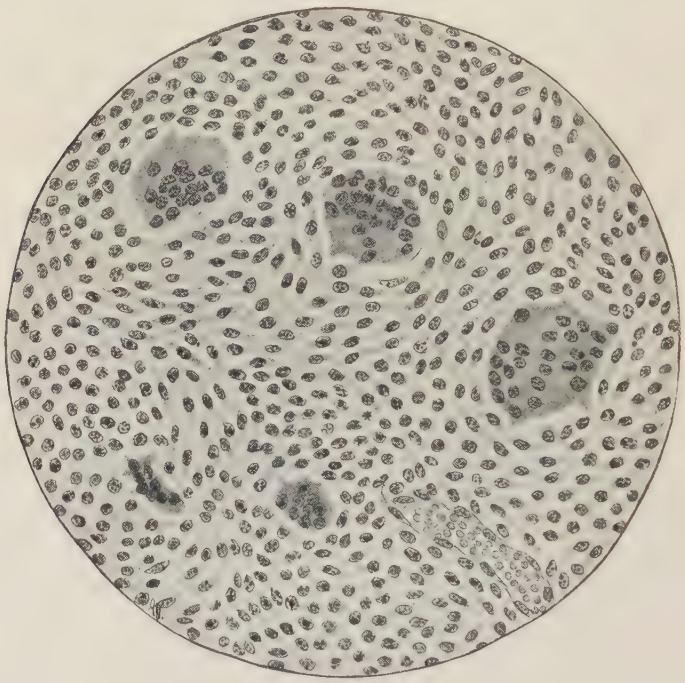

FIG. 313.—Giant-cell tumor, showing several large multinucleated cells of the foreign-body type.

They possess numerous small oval nuclei, which are situated towards the center of the cell, and not around the periphery or at one end as is so commonly seen in tuberculosis. The cytoplasm is opaque and stains deeply. These cells, whose function is probably destructive, are regarded by some as osteoclasts, but it appears more probable that they are endothelial cells.

It is important to note that giant cells may also occur in malignant osteosarcomas. These latter cells are true tumor cells, not foreign body giant cells. The cytoplasm stains faintly, and the nuclei, which are less numerous are large, vesicular, and may show lobulation.

In some cases there are large cells which are loaded with doubly refractive lipoid, probably cholesterol ester. These are often called xanthoma cells, because the lipoid is similar to that found in xanthoma. They are found particularly in tumors of tendon sheaths.

The giant-cell tumor is not accompanied by any marked symptoms until the weakening of the bone makes itself felt. Spontaneous fractures are of frequent occurrence. Indeed it is such a fracture which may bring the patient to the surgeon for the first time.

The importance of conservative treatment is now well recognized, although in the past the name of sarcoma has been responsible for the

FIG. 314.—Multiple myelomata in the skull.

loss of many limbs. Thorough excision or curetting, as Bloodgood in particular has emphasized, is all that is required.

Multiple Myelomata.—This is a curious and rare condition, chiefly affecting males of middle age, with the formation of multiple tumors in the bone-marrow, enlargement of the spleen in many cases, the appearance of Bence-Jones albumose in the urine, and a progressive asthenia which finally terminates in death.

The tumors are primarily multiple, principally involving the ribs, sternum, vertebræ, and skull, although other bones may also be affected. The growths are small, soft, hemorrhagic, and after perforating the periosteum may invade the soft parts. Spontaneous fracture is a common occurrence.

The albumose is found in the urine in about 50 per cent of the cases. It may be present on some occasions and absent on others. It doubtless bears some relation to a somewhat severe nephritis which is commonly present, but it has been suggested that it may be derived from the elastic tissue of bone. It appears when the urine is heated to 55° C., disappears at 85°, but reappears on cooling.

The blood seldom shows any marked changes apart from a progressive anemia, but both myelocytes and plasma cells have been described.

The *microscopic picture* is a varied one. In some cases the tumor is composed of plasma cells, in others of round cells resembling lymphocytes. The numerous variations which occur in rare cases cannot be considered in a work of this scope. A full discussion will be found in Ewing's book on Neoplastic Diseases.

The origin of the cells is another subject regarding which much has been written but little is known. The bone marrow cells of various types must be regarded as the parent cells.

The Diagnosis of Bone Sarcomas.—It has been the usual practice in cases of bone tumor the nature of which was in doubt to excise a small portion for microscopic examination. It is well that the surgeon should recognize the pitfalls of this procedure. An atypical piece may be removed or one which is gravely altered by inflammatory or degenerative changes. This is more true of bone sarcomas than of tumors of other tissues owing to the confusing variety of histological features which they may present. In this more than in any other field of microscopic diagnosis it is essential to take all the clinical facts into consideration. Even an observer of such wide experience as Professor Ewing remarks that "the more experienced the pathologist, the more he learns to rely on clinical data for clinical diagnosis, and the more he urges the surgeon to make his diagnosis on clinical observation, and not to expect too much from the study of small pieces of tissue."

A diagnostic incision of a malignant bone tumor is not without its dangers in the matter of dissemination. If a giant-cell tumor is to be treated by radiation it is very important that the skin and the tumor capsule should not be incised for diagnosis, for the scar may break down under repeated radiation, and infection of the tumor may result.

The use of the X-ray and of radium has placed in the hands of the surgeon a potent means of diagnosis, and the great majority of bone sarcomas can be diagnosed by these means. The therapeutic test affords conclusive evidence of the nature of certain tumors of bone. Myelomas and diffuse endotheliomas in particular melt away under radiation. The giant-cell tumor is affected more slowly, but the growth is held in control, and the shaft gradually restored. Osteogenic sarcomas do not respond to radiation.

With regard to the X-ray picture, Ewing summarizes the matter as follows: "Osteogenic sarcoma almost never affects the middle half of the shaft, but is a disease of diaphyseal ends; erosion or destruction of a segment of shaft is nearly constant in osteogenic sarcoma; the benign central tumors regularly widen the shaft and displace the periosteum with its thin shell of bone, long before more aggressive forms of this disease invade the soft tissue; the myelomas and diffuse endotheliomas involve wide segments of the bone, often the midportions, and cause smooth gradual fading of the shaft. Syphilis, tuberculosis, chronic osteomyelitis and periostitis, and Paget's disease, each presents its own peculiar morphology and clinical setting, and, with rare exceptions,

FIG. 315.—Carcinomatous deposit in bodies of vertebræ secondary to carcinoma of breast.

lacks the specific features of bone tumors. It must be admitted that these interpretations require experience; but no inexperienced person should undertake to deal with bone tumors. When the experienced observer is unable to reach a conclusion, then resort must be made to the diagnostic incision before amputation is advised."

Secondary Carcinoma.—Metastatic deposits in bone from a primary glandular carcinoma are of fairly frequent occurrence. The most frequent sites of the primary tumor are the entire genito-urinary system, the breast, the thyroid, and the adrenal. In the genito-urinary system the prostate easily takes the first place, but renal hypernephroma and renal carcinoma both exhibit this tendency to a marked degree, and the same is true to a lesser extent of papilliferous

carcinoma of the renal pelvis, and even of the similar tumor of the bladder. Joll in a Hunterian Lecture cites rarer instances of primary tumors in the testis, tongue, esophagus, stomach, and large intestine. Reference has already been made to the curious metastases in the skull from neuroblastoma of the adrenal medulla (page 434). The bones most often affected by secondary carcinoma are the humerus, radius,

Fig. 316.—Carcinomatous deposit in left humerus secondary to carcinoma of breast.

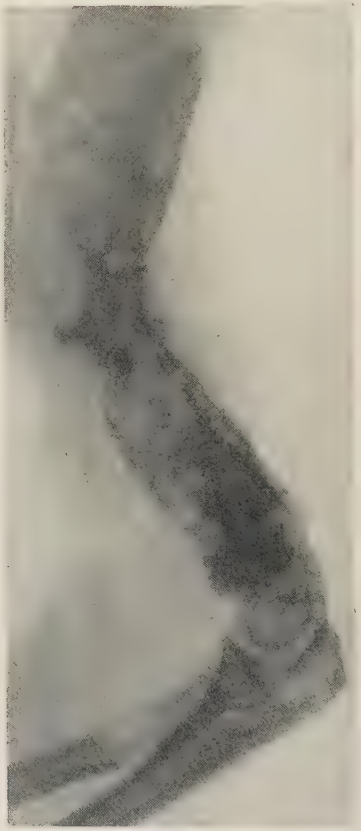

Fig. 317.—Right humerus almost entirely replaced by carcinomatous growth secondary to carcinoma of breast. Pathological fracture.

ulna, skull, vertebral column, ribs, pelvis, femur, and the bones of the foot.

The deposit is formed in the medullary cavity, and may closely resemble the parent growth, which may itself be unsuspected. Thus a tumor removed from the humerus showed the structure of a hypernephroma, and when the patient died some months later a hypernephroma was discovered in the kidney. The first indication of the presence of a tumor may be a spontaneous fracture. Such an occur-

rence in an old man should lead one to make a careful examination of the prostate.

Cancer of the thyroid may give rise to metastases in bone, and the secondary growths may reproduce the normal structure of thyroid tissue to perfection. Still more remarkable is the fact that in some cases of multiple thyroid tumors of bone the thyroid itself has shown nothing but an ordinary adenoma without a trace of any malignant characters. This extraordinary condition has been called general thyroid malignancy.

Bone may become involved in a carcinomatous process through spread of the disease from the adjacent soft parts. An epithelioma

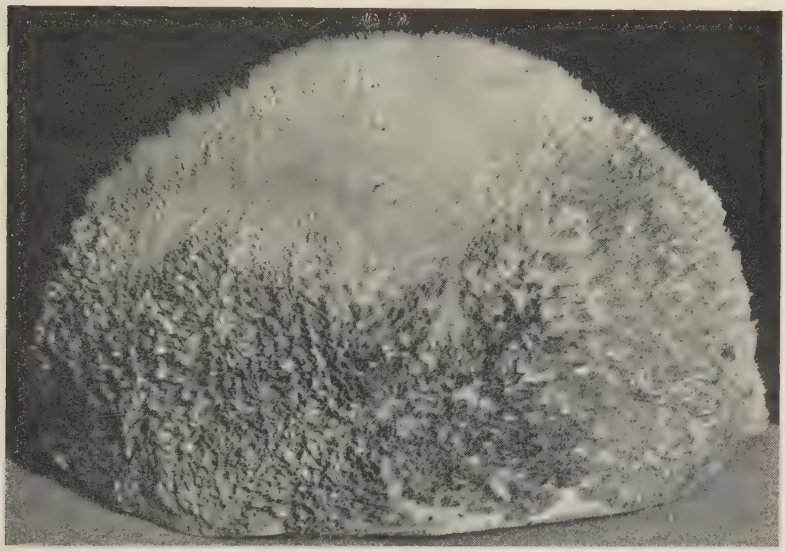

Fig. 318.—Metastases in skull from neuroblastoma of adrenal medulla.

of the mucous membrane of the mouth may invade the jaw or the palate. Or an epithelioma may commence in a sinus communicating with bone, and eventually involve the bone itself.

Fibromas of bone are usually found in connection with the bones of the face, especially the superior maxilla. The tumor may form a nasopharyngeal polypus with ulceration of the mucosa. It grows from the periosteum.

Myxomas are very rare. They may arise from the periosteum or the marrow.

Angiomas have on rare occasions been found in the vertebræ, the skull, and the sternum.

OSTEITIS DEFORMANS

Paget's Disease of Bone

This rare and interesting condition, the exact nature of which is still unknown, was first described by Sir James Paget in 1876. The

essential feature of the disease is an associated softening and overgrowth of bone. Persistent bone pains form the chief subjective symptom in the earlier stages.

Clinical Features.—The bones principally affected are the skull, the vertebræ, and the bones of the leg, but almost any bone in the body many be involved. As a rule the disease manifests itself in a number of bones, but in rare cases it may be confined to one bone; the diagnosis is then a matter of great difficulty.

The bones of the lower limbs are usually the first to be affected, but in a number of cases the disease may commence in the skull. The softened bones of the leg, having to bear the weight of the body, become bent; the femur bends outward, the tibia forwards. The patient therefore becomes bow-legged. In addition to the bowing there may be a marked twisting, so that, as DaCosta remarks, the femur comes to look as though it had been grasped by the hands of a giant, bent into a bow, and then twisted. Other factors in addition to that of body

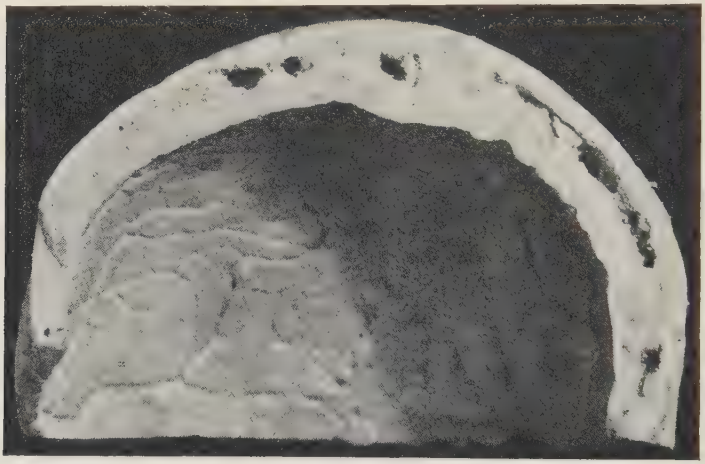

Fig. 319.—Paget's disease of the skull. Although the skull is so thick, it is also quite porous, and water runs through it with the greatest ease.

weight must be responsible for the deformity, for the bones of the arm also become bent, although to a lesser degree. In this case the curve is backward.

Associated with the bending, or even before it occurs, there is a very characteristic thickening of the bone. The bone pains which are so constant a feature of the disease are felt particularly in the legs, seldom in the arms or head. They may be continuous or periodic. The bone pains may appear many months before any gross lesion can be detected.

Enlargement of the skull is almost always present at some stage of the disease. It may be the first sign to appear, and may first attract attention through the patient noticing that he has to buy hats of

ever increasing size. The deformity in typical cases is so characteristic that it can be recognized at a glance. The head becomes a triangle with the base above; the face usually escapes almost completely. The enlargement is due to an enormous deposit of bone on the outside of the cranium; there is no endocranial thickening. To those cases in which the facial bones and the skull are thickened whilst the other bones escape the name *leontiasis ossea* is given.

The vertebral column is almost always involved, and a marked kyphosis develops in the dorsal and lower cervical regions. As a result of the kyphosis the patient shrinks in height, an occurrence which is aggravated by the bowing of the legs. There are cases in which a man has lost as much as a foot in stature.

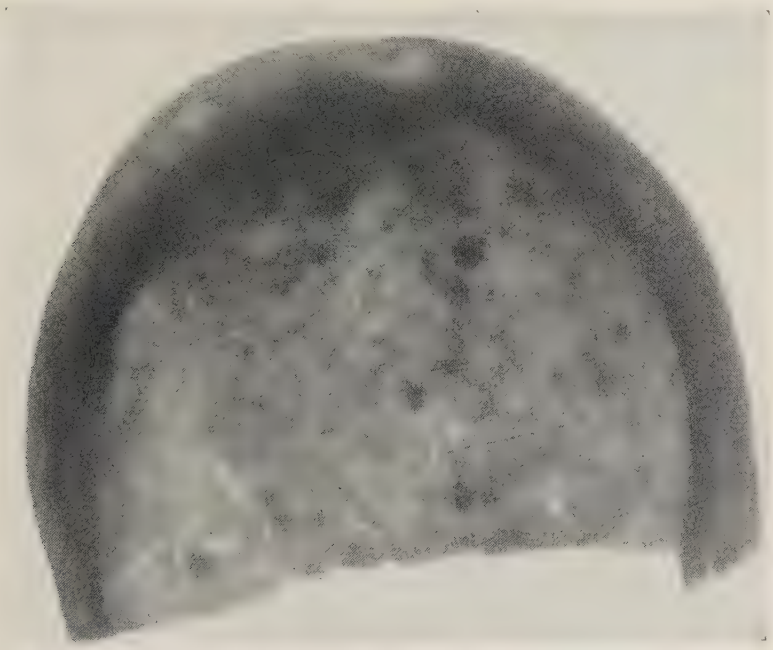

FIG. 320.—Paget's disease of the skull associated with sarcomatous deposits.

The clavicles may be affected, and in exceptional cases the bones of the hands and feet. The pelvis may be broadened, the ribs thickened, and the chest deformed.

The X-rays show characteristic changes long before any deformity appears. There is great thickening and increase of density of the bone, and the vault of the skull presents a peculiar serrated appearance. An X-ray picture should be made in all patients with chronic bone pains.

The appearance and gait of the patient in the advanced stages is highly characteristic. The short squat figure with the bent shoulders, the curved back, the sunken chest, the long arms, and the great head

hanging forward, waddles along with bowed legs, out-turned toes, and the aid of a stick, the living justification for the term osteitis deformans.

The disease is slowly progressive, but may not shorten life, and is compatible with unimpaired mental activity.

Etiology.—The cause of Paget's disease of the bone is unknown. Paget himself regarded it as a chronic inflammatory condition. French workers consider that it is a late manifestation of syphilis, congenital or

FIG. 321.—Paget's disease of the tibia, showing bowing and altered density.

acquired. There appears to be a relationship between Paget's disease and osteitis fibrosa cystica; indeed by some the two conditions are regarded as identical.

In this age it is only natural that the view should be expressed that the condition is due to disorder of the ductless glands. The undoubted relation of the pituitary gland to acromegaly lends consider-

able support to this view. Hawk has demonstrated metabolic changes of importance. There is a marked retention of calcium, magnesium, and phosphorus, and a large elimination of sulphur. It has been suggested that during the formation of new bone the matrix of the osteoid tissue is abnormally rich in sulphur. As calcification proceeds the sulphur is replaced by calcium, magnesium, and phosphorus, and is then excreted in the urine.

The suggestion by Cole that the primary lesion is a cardiovascular one is considered below.

Pathology.—In the early stages of the disease the bones are so soft that they can be cut with a knife. Later they may become extremely hard. As already indicated the essence of the disease is bone absorption associated with or followed by increased bone formation.

The bone absorption leads to great enlargement of the Haversian canals. In Paget's original specimens there were innumerable apertures for vessels, and the whole skull was finely porous. Cole, in a recent paper on the pathology of Paget's disease, lays great stress on the vascular changes in a case which he examined. The vessels in the bones showed varicosity, thrombosis, congestion, hemorrhage, and leakage with edema. Cole says: "My impression is that we have a primary blood vessel pathology like one sees in syphilis, hereditary or acquired, with accompanying bone changes." The vascular lesions he considers infectious in origin.

Absorption is followed by the formation of new osteoid tissue, soft and pliable at first, but later becoming rigid through the deposition of lime salts. The new bone is chiefly deposited from the periosteum, but a slight deposit may take place from the medulla.

The medullary cavity becomes obliterated, although not by the formation of any dense bone. It is filled with a vascular fibrous tissue which may produce soft osteoid tissue. The diplœ of the skull disappears and the distinction between the outer and inner tables is lost.

Paget's disease is a strong predisposing cause towards the development of sarcoma of bone. This has occurred in nearly 10 per cent of the recorded cases.

OSTEITIS FIBROSA CYSTICA

This rare condition was first described by Von Recklinghausen in 1891, and is sometimes known as Von Recklinghausen's disease, an undesirable term which should be confined to the multiple fibromata occurring upon the cutaneous nerves. The disease consists in the formation of new vascular connective tissue which may soften and give rise to cysts. Bloodgood and others consider that the condition is essentially an inflammatory one, a low-grade form of osteomyelitis. On the other hand there is evidence to suggest that this is one of those obscure disorders of calcium metabolism and ossification of which Paget's disease, osteomalacia, achondroplasia, rickets, and hereditary multiple chondromata (hereditary deforming chondrodysplasia) are

other examples. In this respect the name of juvenile osteodystrophy is quite appropriate.

Clinical Features.—The disease is essentially one of early life. Most of the cases occur between the ages of 10 and 20, but in Bloodgood's series one patient was only 2½ years old. Cases after the age of 20 are almost unknown, and if occurring later in life are likely to be examples of Paget's disease or osteomalacia.

The symptoms are by no means proportionate to the degree of bony change. Of the three principal symptoms—pain, swelling, and fracture—pain is rarely a prominent feature and the swelling occurs late.

Fig. 322.—Osteitis fibrosa cystica of the femur complicated by sarcoma.

Very many patients come for the first time complaining of spontaneous fractures. Owing to the softening of the bones which are very poor in lime there may be bowing of the arms and legs, and these deformities are often very angular and irregular. The bones most commonly affected are the humerus, the femur, and the tibia in the order named. The jaw, the skull, and the bones of the trunk may occasionally be involved. There are two main clinical types, the localized in which one bone is affected, and the general in which a number of bones

are attacked. The latter is quite rare, there being only 4 cases in Bloodgood's series of 69.

The X-ray picture of the cysts is very striking. The clear area is often continued down the shaft as a pointed extension; in other bone cysts, such as those which occur in giant-cell tumors, the lower limit is rounded.

The disease is of long duration, and may be complicated by the development of the relatively benign giant-cell tumor.

FIG. 323.—Osteitis fibrosa cystica in the neck of the femur associated with ossifying sarcoma.

Morbid Anatomy.—The medullary tissue is replaced by new connective tissue with or without cyst formation. It is important to note that the cyst formation, the dramatic feature of the disease, is by no means essential. In this respect the condition resembles the so-called multiple cartilaginous exostoses in which the development of exostoses is interesting but incidental.

The main pathological features are a general and diffuse degeneration and absorption of bone, a growth of vascular connective tissue, cyst formation, the rather frequent development of giant-cell tumors, and spontaneous fractures. The cysts are usually small, but may attain a considerable size (Figs. 322 and 323). The wall of the cyst may become greatly thinned, and in the case figured in the text it was in places thin

as parchment, so that the slightest trauma was sufficient to produce a fracture. The cysts are lined by fibrous tissue. The fluid contents of the cysts are never distinctly hemorrhagic; they are usually thin, dark brown in color, and show a few blood cells microscopically. Frequently, however, the cysts are filled with gelatinous or fibrous masses rather than with fluid.

The bones are remarkably porous, so that curvatures and angular deformities are fairly common. Sections of the bone show a bony meshwork enclosing vascular marrow-like tissue. The compact bone may have largely disappeared.

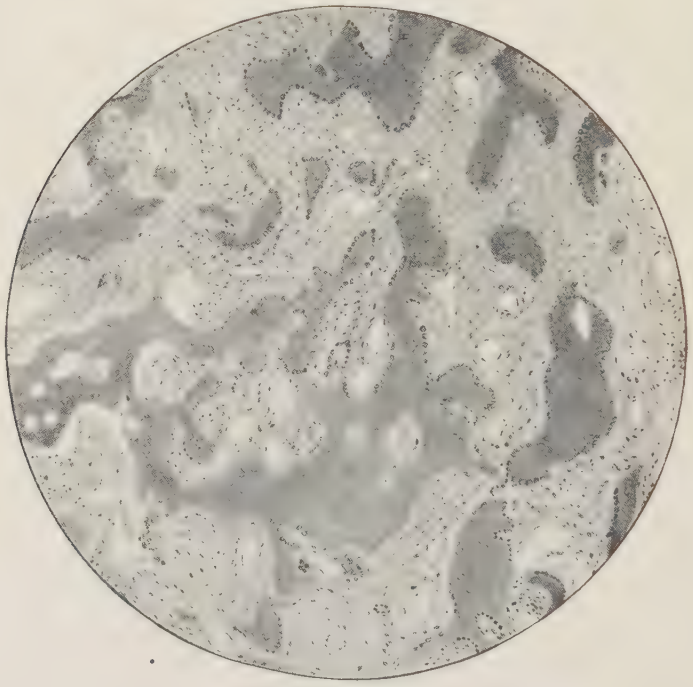

FIG. 324.—Osteitis fibrosa cystica, showing absorption of the bone and replacement by granulation tissue.

In a considerable number of cases osteitis fibrosa is complicated by the development of a relatively benign giant-cell tumor. Giant cells are found even more frequently in the walls of the cysts and in the new connective tissue. In one of our own cases tumor growth began after the disease had existed for a number of years, but in this case the tumor was not of the giant-cell type but an ossifying sarcoma which killed the patient.

Bone cysts occur as a complication in many diseases of bone. Bloodgood gives the following list in addition to osteitis fibrosa cystica: multiple chondromata, myxoma, giant-cell sarcoma, osteitis deformans, subperiosteal hematoma with a bony wall due to an ossifying

periostitis, and callus cysts. To these may be added bone abscess, echinococcus cysts, and osteomalacia.

OSTEOMALACIA

This disease is of extreme rarity on the North American continent, but is fairly common in the Rhine valley and in Northern Italy. Numberless theories have been suggested to explain the condition, but it is probable that, like rickets, it is a deficiency disease due to the lack of some vitamine in the food.

The disease is one of middle life, and it is almost confined to women, especially those who are pregnant or who are exhausted through bearing large numbers of children. Many bones may be affected, but those exhibiting most the effect of the disease are the lumbar vertebræ, the pelvis, and the bones of the legs.

All the symptoms are due to a decalcification of bone, the lime salts being removed, the organic part left uninjured, so that the bone can be bent, cut, and sometimes actually squeezed like a sponge. An excess of lime salts is excreted in the urine and the feces. The bone marrow is extremely vascular. The periosteum may occasionally lay down new bone on the surface, but there also calcification is very incomplete.

The vertebræ become compressed, so that the patient may rapidly lose height. Softening of the pelvis may lead to a deformity which may make normal delivery impossible. The promontory of the sacrum comes forward, and the pressure of the head of the femur drives the acetabula inwards, so that the pelvic inlet is greatly distorted and narrowed. The thorax is compressed laterally. In the leg the bones are curved forwards and outwards. In its effects, therefore, as well as in its nature and causation the disease bears a distinct resemblance to rickets.

ACHONDROPLASIA

Another disease which bears some resemblance to rickets is achondroplasia, sometimes called fetal rickets. It affects bones developed in cartilage, that is to say the long bones and the base of the skull, whereas the bones of the face, developed in membrane, escape. The essential basis of the condition, as the name implies, is a malfunctioning of the epiphyseal cartilage, so that the long bones do not increase in length, and the result is a stunted dwarf with short arms and legs. The epiphyses are enlarged, and with the short diaphysis the appearance of a long bone has been likened to a collar stud. The head is large, the bridge of the nose depressed, the hands and feet squat, the fingers of equal length—the so-called "trident hand."

The cells of the epiphyseal cartilage show no sign of proliferation, and although enlarged are not arranged in definite rows.

The cause of the condition is unknown, but may well be due to defective secretion on the part of one of the ductless glands which regulates skeletal growth.

HEREDITARY DEFORMING CHONDRODYSPLASIA

This remarkable condition is known by a variety of other names, such as multiple cartilaginous exostoses, hereditary multiple exostoses, and multiple congenital osteochondromata. As the names imply, these terms indicate that the disease is sometimes regarded as a form of neoplasm, sometimes as a hereditary disturbance of the metabolism of cartilage and bone.

Clinical Features.—The disease, which is about three times as common in males as in females, begins in early life. It is characterized by the appearance of multiple growths in the bones. These growths, however, are merely incidental, not the essence of the disease. They are as a rule first noticed during the first decade of life. Almost any bone in the body may be involved, but those affected are, in their order of frequency, the femur, tibia, humerus, fibula, radius, ulna, phalanges, ribs, scapula, and pelvic bones. It will be noticed that the flat bones as well as the long bones may be affected by the disease. The bones of the face and skull are rarely involved; they are laid down in membrane, not in cartilage.

The changes to be observed may be divided into two main groups: (1) growth retardation, and (2) proliferative changes.

Growth retardation may affect the form, length, and thickness of the bone. This may best be seen in the metacarpal bones. The different metacarpals may vary markedly in size and shape, and this is particularly true when X-ray pictures of the two hands are compared. Similar changes are seen in the scapulæ and pelvic bones. The acromial process may be very large, the body and glenoid process very small. In most cases the bones attain to a normal length, but they remain thin and delicate. Such bones as the radius, ulna, tibia, and fibula may show a considerable amount of bowing, due probably to unequal growth of the two bones. Cyst formation may be visible in the X-ray picture. In a case of Carman's there were large cysts in most of the lesions, and the upper part of the shaft of the humerus was entirely cystic on both sides. The stature is stunted, owing to the short legs. The under development of the fibula may give rise to a condition of pes valgus, that of the radius may cause a marked deformity of the wrist with ulnar deviation.

Proliferative changes are to be observed both distal and proximal to the epiphyseal line. The early disappearance of that line itself is a striking feature of the X-ray picture. In the *epiphyses* there is enlargement and distortion of the bone. The neck and great trochanter (but not the head) of the femur, the condyles of the femur, and the head of the tibia may show great enlargement, but no definite outgrowths. In the head of the fibula and the acromial process of the scapula, on the other hand, distinct growths, epiphyseal in origin, may occur.

Changes in the ends of the diaphysis are well seen at the lower end of the femur and at both ends of the tibia. They consist of curiously

shaped outgrowths, sometimes stalactite-like in form, which may encroach upon the epiphysis, but originate in the diaphysis.

In the shaft of the diaphysis the common change is the appearance of a number of definite exostoses or of nodular partially organized swellings of the periosteum. The growths often appear as the result of an injury to the bone. It appears as if the bone were specially sensitive to injury, and reacts in this way. The nodules may gradually disappear, or may become completely ossified. The relation of the exostoses to the deformities due to retardation of growth is variable. In some forms of the disease the exostoses never develop. In other cases exostoses may appear in bones which show no deformity, whilst some of the deformed bones may show none.

The disease ceases when skeletal development is complete. The patient usually comes to the surgeon about the age of puberty because of pes valgus, pressure symptoms, or general bone pains.

Pathology.—The nature of the disease appears to be a disturbance of bony metabolism occurring early in life, and it may be *in utero*. The metabolic studies of Honeij are worthy of note. This observer found that "in the stabilized stage of the disease calcium exchange differs little from that of a normal individual, whether the abnormal subject is maintained on a calcium poor or a calcium rich diet. In the progressive stage of the disease calcium metabolism is markedly different from the normal in that calcium is lost from the body." Nests of cartilaginous cells may be left under the periosteum covering the ends of the shaft. These remain uncalcified, but at a later date they may develop into cartilaginous exostoses or chondromas.

FRAGILITAS OSSIUM

Undue fragility of the bones may occur as a complication of fetal life, or may not appear until the patient has grown up. The congenital form is known as *osteogenesis imperfecta*. Many fractures may occur *in utero*, and if not they are certain to take place at time of birth. The skull presents a remarkable condition, for the vault is made up of a large number of small fragments pieced together in mozaic fashion, and separated by unossified membrane.

The adult form, as also the congenital, is frequently familial. I have studied a family in which six members suffered from multiple fractures, and there were several other victims on the mother's side. In this case the calcium content of the urine was below normal.

In both forms the bones are light, porous, and rarefied, so that fractures may occur on the slightest provocation. There must be some disturbance of calcium metabolism, but its exact nature is quite unknown.

OSTEOCHONDRITIS DEFORMANS

It is only within the last dozen years that this condition has come to be recognized. Nomenclature and priority claims both present knotty problems which need not be entered into here. One of the

first to recognize the condition as a distinct entity was Legg of Boston, who described 5 cases in 1909. Next year Perthes, of Tübingen, published a careful account of the condition which he has followed up by a series of papers, and the disease is frequently known as Perthes' disease. Other names commonly employed are pseudocoxalgia, osteochondritis deformans juvenalis, and epiphysitis of the head of the femur.

Clinical Features.—Most of the cases occur between the ages of 5 and 10; the disease is unknown after the age of 15. It is commoner in boys than girls; in one series of cases the proportion was as four to one. A history of recent injury is often given. The earliest sign is a

FIG. 325.—Perthes' disease: extreme flattening of the head of the femur.

limp, usually accompanied by little or no discomfort, although occasionally there may be pain in the hip or knee. There is slight restriction of mobility affecting the movements of abduction and internal rotation. There is little or none of the atrophy of the buttock and thigh so characteristic of tuberculous disease of the hip, nor is there any thickening of the soft parts overlying the joint. A mild degree of irregular pyrexia is not infrequently present. The picture is that of a mild transient synovitis of the hip joint. After a varying period the symptoms disappear. Two signs, however, persist during life, thickening of the trochanter and limitation of the range of abduction.

The X-ray picture is absolutely characteristic, and it is by means of it that a final diagnosis is made. The head of the femur is distorted and flattened, and the neck is broadened and stunted. The acetabulum becomes altered to conform with the final shape of the head. Where the discrepancy in size is great the acetabulum is shallow. A full discussion of these matters will be found in Platt's paper.

Morbid Anatomy.—Very few opportunities have presented themselves for an examination of the diseased tissues. The most important contribution is that of Phemister, who removed a portion of the head of an affected femur. The joint cavity showed evidence of an acute synovitis, but the articular surfaces retained their normal sheen. The center of ossification of the epiphysis was broken down, forming a cavity which was filled partly with granulation tissue, partly with necrotic débris and a number of small sequestra. Cultures and animal inoculations proved negative. Histological examination suggested an old, probably pyogenic, infection which had destroyed most of the head of the femur. The restricted nature of the infection would be accounted for by the fact that the center of ossification is everywhere surrounded by a wall of cartilage which resists the spread of the inflammatory process. As this layer of cartilage is not pierced by nerve fibers the center of ossification has no nerve supply, which would account for the absence of pain.

Etiology.—Many suggestions have been made regarding the essential cause of the disease. *Trauma* is a factor frequently mentioned. Legg considers that it is the sole determining factor, that the injury causes an obliteration of part of the blood supply to the epiphysis which accordingly atrophies, whilst a compensatory hyperemia of the neck leads to corresponding thickening. This somewhat fantastic hypothesis has little to support it. *Rickets* has also been suggested as a causal factor, but with even less foundation. Needless to say, endocrine dysfunction has been dragged in to explain this obscure condition, and as usual without the slightest justification.

The theory that the disease is due to a low-grade infection is the most probable one. The occasional occurrence of pyrexia would bear this out. The pathological findings of Phemister agree with it. Trauma may well determine the occurrence of the disease in the hip, just as it plays an important part in the production of osteomyelitis elsewhere.

KÖHLER'S DISEASE OF THE SCAPHOID

Brief reference may be made in this place to another condition simulating tuberculosis but essentially innocent, first described by Köhler in 1908.

A child, usually between the ages of 4 and 8, develops a limp, and complains of discomfort or actual pain at the site of the scaphoid. The X-ray picture shows that the scaphoid is diminished in size, biconcave, and of irregular density or actually opaque.

Both the pathology and etiology are unknown, but they may be similar to those of Perthes' disease. Many of the cases give a history of trauma. Ossification of the scaphoid does not commence till the age of four, and it is possible that trauma or some other unknown factor may cause enlargement of the bone, and that the antero-posterior pressure spreads out the softened and enlarged bone into the form of a biconcave disc.

Fig. 326.—Köhler's disease. The difference in the condition of the scaphoid on the two sides is well shown.

The prognosis is excellent, as recovery rapidly occurs when the weight is taken off the foot combined with immobilization.

RICKETS

Rickets is a constitutional disease making its appearance about the age of six months and continuing it may be for several years. The active period of the disease is during the first two years, but its effects may accompany the patient during the remainder of his life. As the most striking features are connected with the osseous system the condition may be considered here.

Clinical Features.—The constitutional symptoms may be pronounced in the more severe cases. Anemia may be marked, and the

sickly-looking, pot-bellied child is liable to acquire any infection that is going about, a feature common to all conditions dependent on a deficiency of vitamine A. There is a general enlargement of the lymphoid tissue throughout the body, and the large spleen is one of the striking clinical features. Other signs that may be mentioned are the flabby condition of all of the muscles (which partly accounts for the pot belly), marked sweating, and delayed eruption of the teeth.

FIG. 327.—Rickets. Extremely irregular line of ossification. (De Lee.)

The interference with ossification, which is so important a feature of the pathology of the condition, is reflected in the very common bony deformities. It is these which persist long after all the active symptoms have disappeared, but in the course of time they also for the most part disappear. Owing to the defective ossification the long bones, especially those of the legs, may bend; the tibia bends forward,

the femur outward. The epiphyses at the wrists, the knees, and the ankles are enlarged. A line of nodules is seen at the junction of the ribs and costal cartilages, the so-called rickety rosary. Curvature of the spine (either kyphosis or scoliosis), the "pigeon breast" due to a forward projection of the sternum, a vertical groove on either side of the thorax or a horizontal groove passing across the ensiform cartilage, are all of common occurrence. The pelvis shows various deformities, notably the flat pelvis; the sacral promontory may be carried forward and the acetabula inward, giving rise to the trefoil appearance seen in osteomalacia. This bony deformity may endanger the life of a woman at the time of childbirth long years after all active signs of the disease have disappeared.

The skull in rickets is characteristic. As the result of a heaping up of spongy bone at certain points bosses of bone are formed, particularly in the frontal and parietal regions. The effect is to make the skull square, and to give to the brow a lofty and intellectual appearance which is seldom warranted. A peculiar lesion may appear at the back of the skull where the head rests on the pillow, for here the bone may become eroded and thinned till it is of parchment-like consistence, a condition known as craniotabes. What relation this lesion can have to the other bone changes in rickets it is difficult to understand.

The X-rays provide a valuable means of diagnosis and of estimating the effects of treatment. The change from the normal narrow line of the epiphyseal junction to the thick irregular line in rickets is very striking. This line may show definite defects of calcification. As the disease progresses decalcification takes place more rapidly at the center than at the periphery; the projecting ends of the compact bone retain their lime salts longer, so that the end of the bone may have a cupped appearance. The method is more valuable for indicating the progress of a case than for diagnosis, for, as Hess points out, by the time that the X-rays demonstrate rachitic changes at the epiphyses, a well defined rosary is almost invariably present.

Morbid Anatomy.—The epiphyseal ends of the bone can be readily cut with a knife. At the points principally affected, viz., the wrist, knee, ankle, and the costo-chondral articulations the epiphyseal line presents a most remarkable difference from the normal. Instead of the normal thin, straight, regular line of ossification there is a wide, irregular band of grey material, which may be as much as 10 or 15 m.m. in diameter, and in which can be seen white streaks of calcified tissue and bluish islands of cartilage. The shaft as well as the epiphyses may show a pathological condition in the shape of deposits of soft spongy bone both on the surface and in the medullary cavity.

Microscopic examination of the epiphyseal line shows that there is an abundant formation of new bone of a sort, but that this new bone is highly vascular and very imperfectly ossified. The cartilage cells are not arranged in regular rows as in normal developing bone, nor does the cartilage become calcified prior to the usual invasion by

Rickets. Rib at site of line of ossification. The preparatory zone of cartilage is irregularly invaded by perichondral and marrow vessels. Calcification of cartilage lacking except in two or three foci. Invading blood vessels surrounded by osteoid tissue. Lamellæ of bone remain partly covered with osteoid tissue (MacCallum).

the marrow vessels. The result is that these vessels invade the cartilage in an irregular manner and to a great distance, leaving long tongues of cartilage projecting towards the medullary cavity. These become converted into thick laminæ of osteoid tissue, resembling bone morphologically, but lacking in the all-important lime salts. The bosses on the skull consist of similar soft osteoid tissue. When the disease is checked lime salts are deposited in the osteoid tissue, which is thus converted into bone.

The periosteal disturbances are similar in character. The periosteum is extremely vascular, and deposits an abundance of new, spongy, poorly calcified bone, ill fitted to stand the strain of the weight of the body and the traction of the muscles. At the same time there is excessive absorption of bone in the marrow cavity, which still further aggravates the condition.

Etiology.—The etiology of rickets has been a subject of discussion for centuries. Much light has been thrown on the subject by experimental methods during the last few years, but the new light has not served completely to dispel the darkness. As the most striking and characteristic pathological feature of rickets is the deficiency of calcium in the bones, it is natural that for many years it was thought that the cause of rickets was a lack of calcium in the drinking water or in the food. This is not the case; animals fed on a calcium-free diet develop osteoporosis but not rickets. Moreover the calcium content of the blood in rickets is normal. The recent experimental work just referred to directs attention to three factors: (1) the fat-soluble vitamin A, (2) phosphorus, and (3) light.

Vitamin A.—It was in 1919 that Mellanby presented to the Medical Research Council a report of the first serious experimental investigation of rickets. Mellanby, working on dogs, came to the conclusion that rickets was mainly due to a lack of the fat-soluble vitamin present in abundance in animal fats such as cream, butter, and eggs, as well as in leafy vegetables. This view seemed the more probable in view of the well known beneficial effect of cod-liver-oil in rickets. Paton and his associates have failed to reproduce these results in dogs, and Hess and his co-workers found that young rats fed on a diet deficient in vitamin A did not develop rickets, although they did develop the keratomalacia which is so constant an eye lesion in this form of deficiency disease. It is to be noted that the animals developed osteoporosis and signs of lack of osteogenesis. It would seem, therefore, that although the fat-soluble vitamin may play a role in the etiology of rickets, there must be other factors involved.

Phosphorus.—Attention has long been focussed upon calcium metabolism in relation to rickets, but it is only very recently that the importance of phosphorus has come to be recognized. In 1921 Sherman and Pappenheimer demonstrated that rickets could be infallibly produced in rats by a diet adequate in calcium but deficient in phosphorus. Indeed so delicate is the reaction that by varying the amount of phosphorus in the food they could vary the degree of

rickets produced. When we come to apply these results to children, however, we are at once in difficulties. The phosphorus content of rickets-producing food is normal. Moreover woman's milk contains only one-fifth as much phosphorus as cow's milk, and yet the former is an infinitely better prophylactic against rickets than the latter. The inorganic phosphate content of the blood is low in rickets, but this change does not necessarily indicate the presence of the disease.

Light.—For centuries it has been known that faulty hygiene apparently bears some relation to rickets. The full realization of the importance of light, however, is of very recent date. In 1920 Huldschinsky showed that infantile rickets could be cured by the rays of the mercury vapor quartz lamp. This has provided a valuable means of studying the disease experimentally, especially in conjunction with X-ray observations. The effect of helio-therapy is a systemic and not a local one, and its value in the treatment of rickets has been proved beyond peradventure. It is of interest to note that rickets is very much more common during the winter than during the summer months.

Deficiency in light and some deficiency in the quality of the food certainly seem to work together in the production of rickets. The one without the other is ineffective. Rats fed on a rickets-producing diet were protected by being rayed for two minutes each day by the mercury vapor lamp, but one minute was found insufficient to prevent the disease. Phosphorus, again, is a factor to be considered.

Short exposures to light may be insufficient to protect an animal on a standard rickets-producing diet, but when 25 mg. per cent of phosphorus is added, the same degree of light affords protection.

Pigmentation of the skin has an influence on the protecting effect of light. Thus white rats on a deficiency diet are protected by a certain exposure to light; for black rats under identical conditions the same exposure is without effect. This explains the great prevalence of rickets among negro children.

The experimental evidence therefore goes to show that these three factors, vitamin A, phosphorus, and light are all of importance in the production of rickets, although how these work together we do not as yet know. For a very full consideration of the etiology and pathology of rickets from an experimental point of view the reader is referred to the recent monograph of Korenchevsky published by the Medical Research Council.

As regards practice, rickets is a disease due to a faulty diet, especially when associated with lack of fresh air, lack of sunshine, and general unhygienic conditions, but the fault lies in the quality rather than the quantity of the food. A starved and emaciated child may show no sign of rickets, whereas a plump well-fed child may show marked evidence of the disease. The disease is confined to bottle-fed babies, except in the case of negro children or when the maternal milk is insufficient owing to prolonged lactation. The exact fault in the diet has not been determined. A diet consisting almost exclusively of carbohydrates or proteins is almost certain to produce rickets. Bland-Sut-

ton showed this in the case of the lions at the London Zoo. Rickets was so prevalent amongst the cubs, fed on lean meat, that not a litter could be reared for years. The addition of cod liver oil and milk to the diet at once abolished the disease.

Rickets can be cured, as has been shown so conclusively by Miss Harriette Chick amongst the famine stricken children of Vienna, by feeding with cod-liver-oil, by sunlight, or by exposure to the radiation of the mercury vapor quartz lamp.

Scurvy-rickets.—Reference may be made in this place to Barlow's disease, which is usually regarded as a form of infantile scurvy developing in rickety children. It is very doubtful, however, whether the disease has any real relation to rickets. In contradistinction to rickets it is usually met with among the children of the well-to-do, children under 2 years of age who have been brought up on artificial and proprietary foods deficient in the necessary vitamines.

There is a marked tendency to hemorrhage both from mucous membranes, the kidneys, etc., and under the periosteum at the ends of the long bones. As a result of the latter lesion the limb is painful, acutely tender, and is used so little as to arouse a suspicion of paralysis. The child screams whenever the limb is touched. Occasionally there is hemorrhage into the joint. The function of the epiphyseal cartilage is interfered with, whether or not on account of the hemorrhagic diathesis one cannot say; the bone ceases to grow in length, and separation of the epiphysis may occur.

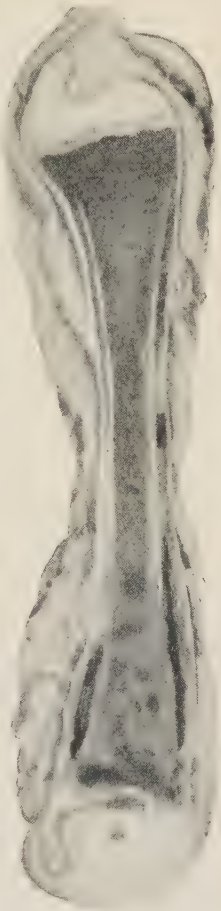

Fig. 328.—Infantile scurvy. Section of femur showing subperiosteal hemorrhages with periosteal bone formation. There are hemorrhages in the bone-marrow and distortion of the line of ossification at the lower end. (MacCallum.)

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CHAPTER XXXV

DISEASES OF JOINTS

A joint is a structure of peculiar delicacy, and one which responds only too readily to injurious stimuli.

The structures which enter into the formation of a joint are the articular surfaces of bone covered by hyaline cartilage, the epiphyses, in some cases the epiphysal cartilage and metaphysis, and the synovial membrane.

Anatomical and Physiological Considerations.—Our knowledge regarding the physiology of joints is still very limited, for a joint is a structure which does not attract the physiological investigator, but the recent experimental work of Timbrell Fisher has brought to light a number of new facts which will be referred to here.

Fisher draws a distinction between the central and the lateral areas of articular cartilage. The central articular area possesses no perichondrium, the surface being formed of clear matrix containing no cells. The lateral articular area is furnished with a delicate perichondrium continuous with the synovial membrane and containing well-marked capillaries. The nourishment of the articular surface is a matter of great importance, for articular cartilage is singularly devoid of blood vessels. There are three probable sources: (1) the capillaries in the subarticular cancellous spaces, which probably supply the deeper layers of cartilage cells; (2) the delicate offshoots to the lateral articular area from the circulus vasculosus, an arterial ring which encircles the joint at the reflection of the synovial membrane and gives off branches to the synovial membrane, the epiphysis, and the metaphysis; and (3) the synovial fluid, upon which alone the superficial layers of the central articular area are dependent. Fisher has shown that the protein content of the synovial fluid is less than half of that of the lymph, and this probably accounts for the feeble powers of resistance of this part of the articular cartilage, the readiness with which it degenerates, and the extreme slowness or absence of repair. He found that in persons between the age of 60 and 70 over 90 per cent showed fibrillation of the central articular area. Experimental destructive lesions of the lateral part are followed by rapid and abundant formation of cartilage, whereas in the central part there is little or none. Moreover, after destruction of the central part there is a marked proliferation of the lateral part which appears to be compensatory in nature, so that the "lipping" which occurs in some forms of arthritis may be an attempt by the better nourished lateral portion to extend the articular surface.

The synovial membrane is lined in the parts more remote from the articular edges by a single layer of endothelial-like cells, but nearer the articular edges this layer is very deficient, so that it offers no obstruction to absorption from the joint cavity. At the margin and especially in the villi which occur chiefly in this region the membrane contains great numbers of cells filled with globules of mucin which can readily escape into the joint cavity owing to the deficiency in the endothelial lining, an escape which is greatly facilitated by movements of the joint. So abundant are these mucinaginous cells in the synovial villi that they have been called "synovial glands." In chronic arthritis portions of the membrane may become detached and continue their secretion within the joint cavity.

Fisher's experimental work on loose bodies in joints has shown that when a piece of articular cartilage is detached, it almost always becomes attached to the synovial membrane, which lays down upon it layer after layer of cartilage. If such a body again become detached it may continue its growth, evidently deriving its nourishment from the synovial fluid, the nutritive value of which is probably increased by the inflammatory exudate.

Injection experiments show that absorption of diffusable dyes from the joint cavity occurs via the capillaries, but that colloidal solutions are absorbed by the lymphatics in the synovial membrane, thus agreeing with what we already know of the general principles of absorption. This absorption is greatly facilitated by passive movements of the joint or by allowing the animal to move about for a few hours. The material absorbed by the lymphatics can be demonstrated in abundance in the abdominal lymphatic glands.

Fraser has shown that when carbon particles are injected into the circulation they tend to accumulate in the region of the circulus vasculosus, more particularly at the lower aspect of the neck of the femur, at the synovial reflection on to the upper end of the tibia, and around the astragalus. A clump of tubercle bacilli may well imitate the behavior of the carbon particles, and as a matter of fact these are some of the commonest sites of tuberculous disease of joints.

In the great majority of cases infection reaches a joint by the blood stream, although occasionally it may be introduced from without either by a wound or by an operation. A hematogenous infection may primarily attack the synovial membrane, or the attack may first fall upon the epiphysis or metaphysis, and later involve the joint itself.

The common diseases of joints are acute inflammation, tuberculosis, gonorrhea, and that peculiar and baffling group of chronic conditions which we designate by such terms as rheumatoid arthritis, osteoarthritis, and arthritis deformans.

ACUTE ARTHRITIS

In considering the somewhat complex subject of acute inflammation of joints the difficulties that beset the way will be considerably smoothed by recalling some of the general principles of inflammation

already discussed in Chapter II. Two of these principles may be restated here. In the first place the two most important causes of inflammation are trauma and bacterial infection. In the second place all forms of inflammation proceed to one of three terminations: (1) resolution; (2) suppuration with tissue death; and (3) repair with fibrosis. By applying these ideas to the particular constituents of any joint we have the pathology of acute arthritis in its varying forms.

Acute arthritis may arise in the following ways.

1. *Trauma.*—A blow, wrench, or sprain will set up an aseptic inflammation confined to the synovial membrane, and usually transient in character. The presence of a loose body in a joint, or a displaced semilunar cartilage in the knee will act in a similar manner.

2. *A perforating wound* of a joint, by introducing infection from without, will give rise to acute inflammation.

3. *Spread of Infection from Neighboring Tissues.*—Inflammation of the adjacent articular end of the bone may involve the joint. That variety known as the acute arthritis of infants is worthy of special mention. Much more rare is spread of inflammation from the soft parts. Suppuration of a bursa or sloughing of the overlying tissues resulting from an injury afford examples of this mode of infection.

4. *Infection by the Blood Stream.*—Any condition in which organisms are circulating in the blood may be complicated by arthritis. The arthritis of *pyemia* forms a familiar feature in the general picture of that disease. Many of the acute infectious fevers may be complicated by arthritis. The organism of *acute rheumatic fever*, although it may attack many other tissues, has a special predilection for the joints. The *gonococcus* may set up an acute arthritis, although a slow proliferative type of inflammation is commoner. The *pneumococcus* may involve the joints as well as the lungs.

If the three possible modes of termination of inflammation be borne in mind it will not be necessary or desirable to discuss simple synovitis and septic arthritis in separate sections. The sequence of events depends entirely on the nature, intensity, and duration of the irritant. It is convenient, however, to distinguish between the mild and the severe forms of acute arthritis.

Mild Form.—A trauma, such as a sprain, or a mild non-virulent bacterial infection will give rise to a synovitis which, as a rule, will terminate in perfect resolution. The arthritis of acute articular rheumatism is somewhat similar in its pathology.

The *synovial membrane* becomes intensely red and congested, affording, should the joint be opened, a striking contrast to the pearly white color of the articular cartilage. An inflammatory exudate consisting mainly of serum with a varying number of leucocytes is poured into the membrane, which therefore becomes swollen, soft, and juicy. As a rule the fibrin-forming constituents do not appear in the exudate, which, on that account, is readily absorbed. Occasionally, however, these are present, and the more plastic and formative type of exudate is less likely to disappear leaving not a trace behind. The epithelial

cells covering the surface are cast off and are found in varying numbers in the joint fluid.

The *synovial fluid* is increased in amount and altered in character. At first clear and translucent, it becomes somewhat cloudy, and is seen to contain floating flakes of fibrin. These may be deposited on the surface of the synovial membrane, so that the latter loses its normal shiny appearance. Desquamated epithelial cells and small numbers of leucocytes are present. The fluid is usually of a reddish tinge, owing to some of the distended vessels in the synovial membrane having given way. The extravasated blood does not clot, but becomes intimately mixed with the synovial fluid.

Under ordinary conditions all the elements of the inflammatory exudate are absorbed, and resolution is complete. Should the joint not be kept sufficiently at rest the condition may become more or less chronic. The synovial membrane becomes permanently thickened and the joint is distended with serous fluid from which little absorption occurs. Melon-seed bodies derived from the original flakes of fibrin may be found in the joint.

Severe Form.—The ordinary bacterial infection of joints is of a more severe character than that indicated in the above description. Owing to thrombosis of the vessels suppuration with tissue death occurs, a condition of acute suppurative arthritis.

The *synovial membrane* is extremely congested, swollen, and so soft as to be almost gelatinous. It loses its epithelial covering and therefore its normal glistening appearance, fibrin is deposited on the raw surface, and the membrane, infiltrated with pus cells, becomes converted into granulation tissue.

The *synovial fluid,* greatly increased in amount, is at first opalescent due to the presence of flakes of fibrin, then milky from admixture with pus cells, and finally becomes frankly purulent. The infecting organisms are often found in the fluid, but not infrequently they are confined to the synovial membrane. Blood may be present owing to rupture of the inflamed vessels.

The cartilage soon loses its pearly-white appearance and becomes ulcerated, so that large areas of the underlying bone may be exposed and every movement is accompanied by excruciating pain. If the arthritis has been secondary to disease in the articular end of the bone the destruction of cartilage is particularly extensive, but even in the form which is primarily synovial there may be marked involvement of the bone. The ligaments become softened and give way, so that dislocation is common and the disintegration of the joint complete. The whole process is merely one of suppuration with tissue death, or in other words abscess formation.

In severe cases the periarticular tissues are frequently involved. The abscess may burst through the capsule of the joint and burrow between the surrounding muscles, sometimes to a considerable distance. It is well to bear in mind that when the capsule gives way and the pus passes into the periarticular tissue the acute symptoms may

suddenly subside in a manner exactly analogous to a ruptured appendix. It is the tension, not the inflammation, which causes the pain, and when rupture occurs both the pain and the swelling may disappear.

It is a curious fact that in cases of pyemia where the joint is distended with pus, oily from breaking down of the subsynovial fat, hardly a sign of inflammation may be found after the joint has been opened and the contents washed away. There is some slight thickening of the synovial membrane, but the cartilage and bone are quite intact.

The result, provided that the patient escapes with his life, is that which invariably follows suppuration with tissue death, namely fibrosis with contraction. The opposing joint surfaces are bound together by adhesions with most serious results to the functional activity of the joint. The anchylosis is as a rule fibrous, but where the articular cartilage has been extensively destroyed there may be cartilaginous or even osseous union.

Acute Arthritis of Infants.—In young children, usually under 18 months of age, an acute epiphysitis is often associated with suppuration of the corresponding joint. The infection begins in the rapidly growing part of the bone, either in the metaphysis or in the epiphysis itself. A small sequestrum is formed, and the pus perforates the articular cartilage and invades the joint. The perforation may be so small as to be quite overlooked, so that in acute arthritis in young children the articular end of the bone must be examined with great care and if necessary explored, even although no communication between it and the joint cavity can be detected.

Pneumococcal Arthritis.—This form of acute arthritis may occur under two sets of circumstances. It may occur as a complication of lobar pneumonia, and is most frequently seen in adults. Or, more particularly in young children, it may occur without any pulmonary involvement, being merely a manifestation of a general pneumococcal septicemia. In the first variety the arthritis appears just after the crisis of the pneumonia. As a rule only one and that usually a large joint is involved, the knee joint being the most commonly affected. The inflammation may advance to any stage, and the joint is usually filled with pus which is of a greenish tinge, lacking in odor, and containing large numbers of pneumococci.

In the variety seen in children the patient is overwhelmed by a pneumococcal septicemia, but in some cases there is an absence of general signs of infection, and the bacteria are apparently carried from some focus such as the tonsil to the joint affected. Pneumococcal arthritis is always a serious complication, and a large number of the cases terminate fatally.

Scarlet Fever Arthritis.—This variety is of fairly common occurrence. In the later stages of the disease, especially in children with severe throat complications, there may be a general suppurative arthritis. At an earlier date, and more particularly in adults, a synovitis may occur chiefly affecting the hand and wrist and closely resembling

articular rheumatism. The lesions are probably due to a streptococcal infection.

Typhoid Arthritis.—An occasional complication of typhoid fever is an arthritis which may remain serous or may go on to suppuration. It occurs late in the disease, and affects one of the large joints, most often the hip. In about half the cases backward dislocation of the hip occurs, owing to distension of the joint with pus and weakening of the ligaments. A polyarticular form is much rarer, and is more likely to be serous in type.

The typhoid bacillus may be found in the fluid, but in a considerable number of cases other pyogenic organisms are present.

Acute Rheumatic Arthritis.—Acute rheumatic fever is so purely medical a condition that discussion of it here would be out of place. Suffice it to say that, acute as may be the local joint condition, it never goes on to suppuration. Although in the main a synovitis, yet in severe cases there is considerable involvement of the subsynovial and periarticular tissues and ligaments. Whilst, therefore, the inflammation clears up completely in the joint affected at the moment in from a few days to a couple of weeks, yet in the more severe cases with periarticular change some degree of fibrosis with corresponding permanent stiffness must be expected. The diplococcus rheumaticus of Poynton and Paine has been repeatedly recovered by those observers from the synovial membrane and the joint effusion, but it is by no means certain whether this is the absolute cause of acute rheumatic fever or merely a secondary invader.

Acute arthritis may occur as a complication in the course of many other infections such as diphtheria, measles, mumps, cerebrospinal meningitis, tonsillitis, etc., but fortunately only on rare occasions. The passage of a catheter or sound may be followed by an arthritis, due to the absorption into the blood stream of organisms from the urethra.

TUBERCULOSIS OF JOINTS

Tuberculosis of a joint may be primary or secondary. It may be primary in the synovial membrane, or it may be secondary to a tuberculous focus in the articular end of the bone. In the young tuberculosis is usually secondary to a focus in the bone, whilst in adults the primary synovial form is much the commoner. The reason for this difference is that in children the growing ends of the bone are highly vascular and the scene of rapid cell proliferation, on account of which they are more vulnerable to attack. In the hip the secondary, in the knee the primary form is usually encountered.

When the spread is from the bone to the joint the primary focus may be situated in the epiphysis, but the metaphysis is more commonly involved. From the latter site the disease spreads to the circulus vasculosus of the joint and thus reaches the synovial membrane. Occasionally, however, it may perforate the epiphyseal cartilage and invade first the epiphysis and later the joint cavity. The tuberculous pus may pour into the joint through a large opening in the articular

cartilage, but usually that opening is quite small and may be no more than pin-point in size.

Etiology.—The disease is most common in children, particularly before the age of six. Occurring more rarely in adult life, it is at the same time more unfavorable in type, and cases occurring above the age of 30 rarely do well. The adult cases are apt to be mistaken, at least in the early stages, for osteo-arthritis, as the principal features are limitation of movement, swelling of the joint, creaking on movement, and slight pain. Tuberculosis both of bones and joints is by no means so uncommon in old age as is generally considered. Sir James Paget, indeed, mentions an example of the disease in a patient 91 years old. This is a point which needs to be emphasized, for many such cases pass undiagnosed because the possibility of tuberculosis has never been considered. The resisting power of these senile cases is very low.

The joints most commonly affected by tuberculosis are the hip and the knee, then the elbow, shoulder, and ankle. The wrist, often diseased in adults, is rarely involved in children. In children the hip is more often affected than all the other joints put together—provided tuberculosis of the spine be excepted.

In not a few cases the onset of the disease is preceded by a local injury, such as a blow or strain. The effect of such a trauma is to produce a local inflammatory exudate or effusion of blood, which provides an excellent soil in which the tubercle bacillus may settle. Diseases such as measles and influenza, which lower the general power of resistance, may act as predisposing agents.

Morbid Anatomy.—Although tuberculosis of a joint may commence either in the joint itself or in the adjacent bone, the end picture is similar in the two cases, so that a common description will suffice, the points of distinction being alluded to as they arise.

The synovial membrane is swollen, voluminous, and so redundant that it not only fills up all the pouches and hollows but occupies the greater part of the joint cavity. In color it is a dirty grey, but may appear cyanosed or plum-colored at operation owing to the action of the tourniquet. The smooth shining appearance of the surface is lost, and a correct diagnosis can usually be made after a glance at the membrane. The surface may be studded with small tubercles, more particularly in the form secondary to bone disease. Often, however, the tubercles are only seen when the membrane is incised. The consistence varies with the degree of connective tissue reaction, but the occurrence of a myxomatous or gelatinous degeneration frequently renders it soft and pulpy, although in the later stages it may be friable. The membrane eventually becomes converted into tuberculous granulation tissue, scattered throughout which are yellow areas of caseation.

The foregoing are the changes most commonly found, but two rare varieties may occasionally be encountered. There may be a great hypertrophy of the synovial fringes, similar to that seen in

arthritis deformans. Or, in rare cases, large tuberculous masses may form, similar to the solitary tuberculomas which are sometimes found in the brain.

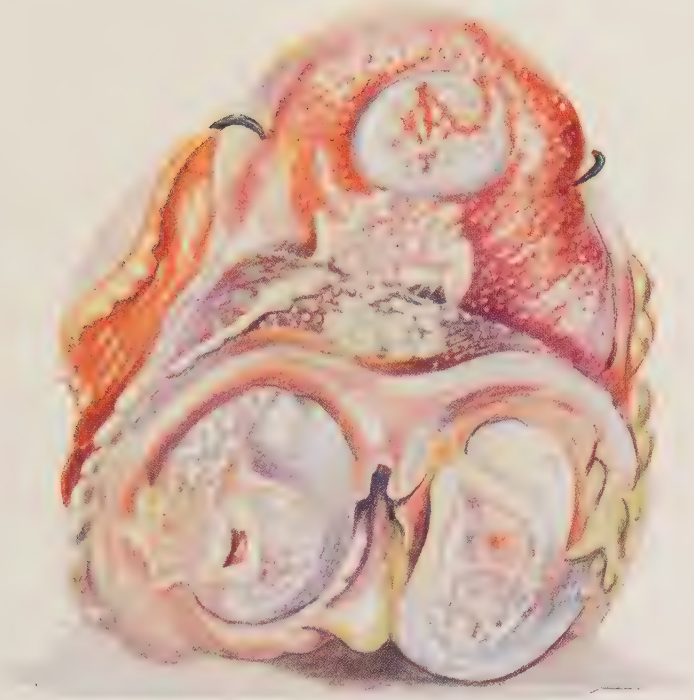
The *contents* of the joint vary. As a rule the cavity is filled with luxuriant masses of synovial membrane, and it is to this, combined with the periarticular changes to be described presently, rather than to distension with fluid that we must attribute the loss of the normal contour of the joint, the disappearance of the bony prominences, and the filling up of the natural hollows. The synovial fluid in such cases is little in excess of the normal, but it contains flakes of fibrin which may be deposited on the surface of the synovial membrane, imparting to that structure a shaggy appearance, or they may give rise to the formation of foreign bodies known as *melon-seed bodies* or *joint mice.*

FIG. 329.—Tuberculosis of head of femur; the articular cartilage has been stripped off.

In a small proportion of cases the joint is filled with a serous fluid, with comparatively little hypertrophy of the synovial membrane, a condition known as *tuberculous hydrops*, and comparable to that form of tuberculous peritonitis which is characterized by the presence of ascites. In other cases there may be a tuberculous empyema of the joint, the fluid which distends the joint being tuberculous and not true pus. The clinical signs of these two varieties may be remarkably similar, so that a correct diagnosis may not be made until an aspirating needle is introduced.

A peculiar and rare form of tuberculous arthritis is known as dry caries or *caries sicca.* It usually occurs in early adult life, and affects particularly the shoulder joint. As the name implies, there is a complete absence of effusion and suppuration, the chief feature being a gradual wasting and absorption not only of the bone but also of the soft parts. There is marked stiffness and pain, but there is no interference with the general health, and the condition may progress to spontaneous recovery, although with permanent stiffness.

The *articular cartilage* becomes involved sooner or later, although, owing to the absence of blood vessels, the disease never begins primarily in the cartilage. The cartilage may be attacked from its superficial or from its deep surface. In the former, which is much the commoner, the diseased and superabundant synovial membrane begins to creep over the articular surface as ivy covers a wall. At first it can be readily separated, but soon it becomes so adherent that it cannot be removed without tearing the surface. The cartilage loses its bluish tint and polished appearance, and becomes opaque



Tuberculous arthritis.

and yellowish. Vessels penetrate from the granulating synovial membrane into the cartilage, producing a series of pits which gives the surface a rough and eroded appearance, so that in time the cartilage also becomes converted into granulation tissue and large areas of bone are laid bare. It is at this stage, when the bone has become exposed, that the "starting-pains" at night appear.

Fig. 330.—An old healed tuberculous lesion of the hip which has left the acetabulum greatly distorted and with numerous exostoses. (MacCallum.)

When the cartilage is attacked from its deep surface the tuberculous process extends from the synovial reflection at the edge of the cartilage inwards between the cartilage and the bone, where a zone of vascular granulation tissue is formed which usually displays very few characteristics of tuberculosis, and the deeper parts of which

tend to become fibrous so as to form a protective cap for the exposed bone. As the process continues the cartilage comes away in flakes, or in exceptional cases the entire surface may be efoliated intact. I have seen a case of tuberculosis of the elbow in which, although when the joint was opened the articular surface showed no trace of ulceration, yet the entire cartilage covering the lower end of the humerus, the trochlear surface of the ulna, and the upper end of the radius could be stripped off as three separate sheets leaving well-covered bony surfaces behind.

The *bone* now becomes the seat of a rarefying osteitis, although naturally in the form which is primary in the bone the osseous changes will already be well advanced. There is no new formation of sub-periosteal bone, and the apparent thickening of the articular ends of

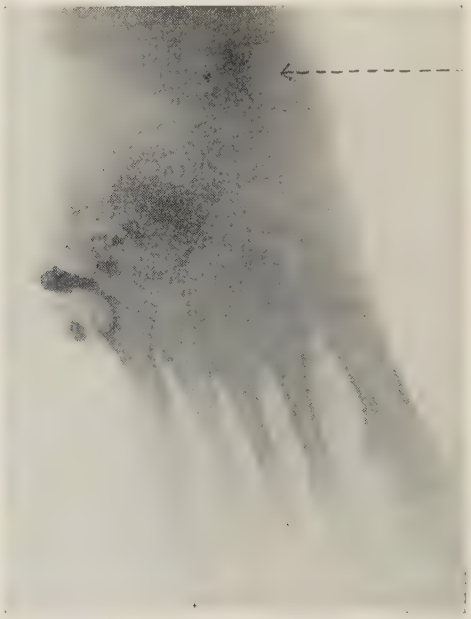


Fig. 331.—Tuberculosis of ankle, with lesions in astragalus.

the bone is entirely due to the changes in the ligaments and the soft parts of the periarticular tissues.

The *soft parts* may be extensively involved. The ligaments become soft and gelatinous and are finally destroyed, as a result of which there is great disorganization of the joint, so that "pathological dislocation" may occur. The muscles, tendon sheaths, and the overlying skin share in this gelatinous degeneration, the result of the tuberculous toxins. This change is responsible for the appearance of the joint to which the name *white swelling* is sometimes applied. At a later date there may be definite caseation of the soft parts, with the formation of a cold abscess which may or may not communicate with the

joint cavity. The fluid contents of such an abscess are not true pus, but rather the product of breaking down caseous tissue, a curdy material mixed with blood serum. Should secondary infection occur, more especially if communication is established with the exterior, a true pyogenic or pus-forming infection will result.

Fig. 332.—Healed tuberculosis of left hip joint, showing osteoporosis, loss of density, and underdevelopment of the bone.

Microscopic Appearance.—The synovial membrane presents the appearance of a granulation tissue in which tubercle follicles are scattered here and there. Giant cells are abundant, the tubercles present a reticulum of epithelioid cells, but cascation may be slight or absent. A tuberculous obliterating endarteritis followed later by a periarteritis is a very constant feature, and is no doubt responsible for the spread of the disease both in the synovial membrane and in the bone, leading as it does to lowering of the resistance of these tissues, whereby they become more vulnerable. Myxomatous degeneration of the ligaments and of the fibrous tissue in the periarticular soft parts is an important feature of the disease, being responsible, to some extent at least for both the softening and the swelling which in many cases are so characteristic.

Terminations.—At any except the most advanced stage of the disease a natural cure may occur. The resulting condition of the joint will naturally depend upon the stage reached by the disease. If only the synovial membrane is affected the subsequent disability may be limited to a slight degree of stiffness. When, however, there has been extensive destruction of cartilage and bone, fibrous or even bony anchylosis may occur.

Acute general tuberculosis is a not infrequent mode of termination in children, but it is remarkable how comparatively seldom phthisis is found in a child with a tuberculous joint.

Amyloid degeneration affecting the liver, spleen, kidneys, and intestine is an accompaniment of long-continued and profuse suppuration. No general rule can be given regarding the length of time that suppuration must be present before the amyloid change makes its appearance. It may come on in the course of a few months. Marsh and Watson mention the case of a laborer in whom, although there had been suppuration of the knee joint and the lower end of the femur for 20 years, no amyloid disease existed.

CHRONIC ARTHRITIS

When we come to the subject of chronic non-tuberculous arthritis we have to sail an uncharted sea, through thick fogs, and with few landmarks that are of any value. At the very outset we are confronted with the problem of nomenclature, a problem almost insurmountable, and certainly not yet solved at the present time. Everyone who writes on the subject appears to consider himself justified in employing a phraseology of his own. Some of the terms such as rheumatic gout and rheumatoid arthritis are absolutely without justification, seeing that the disease bears no relation either to gout or rheumatism, but the latter term is of such everyday use that it is difficult to dispense with it.

It is more than probable that we are dealing with a number of different diseases, which in due time will be differentiated from one another. In speaking of disease it must be remembered that our conception is rather one of varying responses to a single cause than a constant and uniform series of pathological and clinical pictures. Moreover in dealing with the diseases of joints it has already been made evident that one exciting cause, such as the tubercle bacillus or the gonococcus, may produce the most varied results, and also that the most varied causes may produce the same end result.

Until, therefore, we know something of the etiology of these conditions—and it is safe to say that at present we know nothing—a satisfactory classification and nomenclature is impossible.

The clinical and pathological evidence warrants us in recognizing two great classes of cases. Often these are typical and clear cut, but borderline forms may occur which blur the outline of the main groups.

The two main groups may be called chronic infective arthritis and osteo-arthritis. The former is commonly known as rheumatoid arthri-

tis, but as it bears no etiological relationship to rheumatism the term is not a happy one. Osteo-arthritis is sometimes used to include both diseases, but it is better to confine the name to that condition in which the lesion is essentially a bony one. Arthritis deformans, when used to include any of these crippling conditions, is a descriptive term which is only too well justified, but it tends to give the impression that we are dealing with one instead of two diseases, and on that account chronic arthritis appears to be preferable.

Nichols divides chronic arthritis into two groups, a proliferative arthritis corresponding to our first class, and a degenerative arthritis corresponding to our second. This classification is made from the standpoint of morbid anatomy, and he emphasizes that the two groups do not correspond to two single etiological factors, that is to say they are not two definite diseases.

The most recent classification is that of Timbrell Fisher, which is as follows:

(1) Synovial Type (O. T. Rheumatoid arthritis). The disease commences and remains more marked in the synovial membrane. The cartilage and bone may be invaded secondarily.

(2) Chondro-osseous Type (O. T., Osteo-arthritis). The disease commences and remains more marked in the articular end, the synovial membrane being involved later.

(3) Mixed Type: The disease commences simultaneously in the synovial membrane and articular end and the changes advance *pari passu*.

Chronic Infective Arthritis

Chronic infective arthritis, commonly called rheumatoid arthritis, usually occurs in women of between twenty and forty. It is not uncommon in children, where it is often associated with, amongst other constitutional symptoms, enlargement of the spleen and of the lymphatic glands. Rarely it may commence in old age.

The attack first falls upon the small joints, especially the proximal interphalangeal and the metacarpophalangeal joints.

The wrist, shoulder, knee and temporo-maxillary joints may be affected. The hip usually escapes. The onset varies in suddenness. As a rule it is gradual and insidious, but occasionally it may begin with an acuteness suggestive of rheumatic fever.

Resolution may occur early, especially as the result of prompt treatment, or the disease may proceed on its progressive and inexorable course to its terrible termination, leaving the patient twisted, gnarled, and crippled for life. The stiffness and deformity are due in part to anchylosis from adhesions between the articular surfaces, in part to contraction of the soft parts preceded by spasm of the muscles.

Swelling of the joint, a very constant symptom, is due to effusion into the joint, but also to a great extent to changes in the periarticular tissues, thus differing in an important particular from osteo-arthritis. The joint has a peculiar doughy feel, and there is no development of

osteophytes at the margin of the bones. The skin over the joint may become stretched and glossy. In addition to the local manifestations of the disease there may be any of the constitutional disturbances described in the next section.

Etiology.—The exact cause of the disease is of course unknown. The list of suggested causes given in the text-books fills one with irritation. Cold and exposure, nervous influences, disorders of metabolism —such suggestions are merely veils for our ignorance. Although no specific organism has been found—indeed there is no reason why there should be a specific organism —the evidence in favor of the disease being the result of a chronic infection is overwhelming. Three points of evidence may be cited in support of this view.

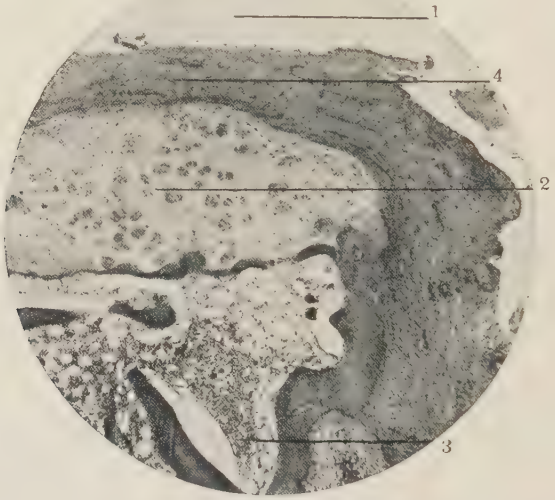


Fig. 333.—Chronic infective arthritis. Photomicrograph of the margin of the articular surface of a phalanx. Shows granulation tissue extending over the joint cartilage from ingrowth of the granulation tissue: 1 shows the joint cavity; 2, the articular cartilage; 3, the shaft of the phalanx. The joint cartilage is covered with a thick layer of granulation tissue, 4, which extends from the synovial membrane over the surface of the cartilage. (E. H. Nichols in Keen's Surgery.)

1. Many of the patients present unmistakable signs of chronic infection. They are pale, pasty, and unhealthy looking; they suffer from malaise, irregular attacks of pyrexia, palpitation, and sweating; their whole appearance is toxic. Occasionally in adults and frequently in children there is enlargement of the lymphatic glands and the spleen.

2. The removal of a focus of infection in the teeth, tonsils, or elsewhere, may be followed by a truly remarkable local change in the joint. In one case which came under my observation there was a chronic arthritis of the wrist presenting the characteristics detailed above. The removal of a tooth at the root of which was a small abscess was followed by a most dramatic flare-up in the wrist, which

lasted for 3 days, and was succeeded by complete recovery. The importance of *focal infection* is of course now generally recognized.

3. Measures designed to combat infection may have a most beneficial effect on the disease. Such a measure is the intravenous injection of a foreign protein, which is followed by a rise of temperature, a marked leucocytosis, and a liberation of defensive ferments and antiferments. A friend of mine, a medical man, had been crippled for several months with chronic arthritis. The joints were the seat of a doughy swelling, and the patient, who presented a typically toxic appearance, suffered from malaise, palpitation, very marked tachycardia, and sweating at night. At the time of the injection he was

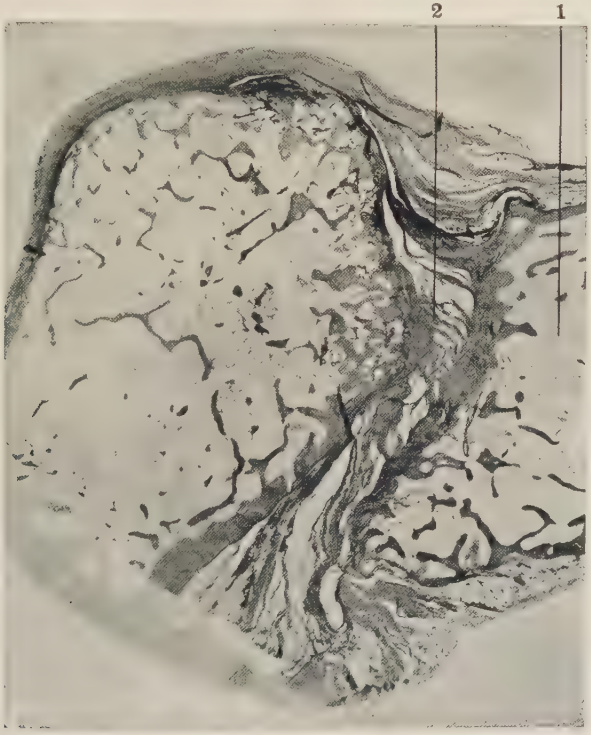


FIG. 334.—Chronic infective arthritis with anchylosis. Photograph of vertical section through phalangeal joint. Shows the distal phalanx, 1, dislocated forward and downward into the palm of the hand; the joint cavity, 2, is practically obliterated and replaced by loose, dense, fibrous adhesions. The joint cartilage has entirely disappeared; the trabeculæ of the phalanges are less numerous and smaller than in normal bone. (E. H. Nichols in Keen's Surgery.)

lying like a log, perfectly helpless, unable to raise his head, and with fingers so swollen that he could hardly move them. The day after the injection he was a new man, he could move every joint of the body without the slightest pain, and the malaise and tachycardia had gone.

It is not suggested that every case is an example of focal infection. The group under consideration will probably be found to include more

than one form of disease. But the evidence is sufficient to apply the term chronic infective arthritis to the majority of the cases. The pathological changes are also those which would be expected to result from the action of a chronic irritant.

Morbid Anatomy.—The process at the commencement is essentially a synovial one, and it may never pass beyond that stage. Thus the disease might be called synovio-arthritis, just as the other main form is called osteo-arthritis. When the joint is opened there is seen to be a great proliferation of the synovial membrane which may form thick pulpy masses, or may present numerous fringes and tags. Marked effusion of synovial fluid contributes to the general swelling.

The synovial membrane may then begin to encroach upon the articular cartilage, forming a thick *pannus*, beneath which the cartilage becomes eroded and ulcerated. The pannus covering the two articular surfaces fuses here and there to form adhesions, and in time the greater

Fig. 335.—Chronic infective arthritis of the hand. Marked ulnar deformity with narrowing of the joint interspaces.

part or even the whole of the joint cavity may be obliterated. The new tissue is usually fibrous, but occasionally it may be cartilaginous or even osseous, and the accompanying anchylosis will be of a corresponding character.

The articular cartilage is not attacked only from its free surface. As a result of the action of the irritant the superficial portion of the epiphysis becomes converted into granulation tissue, and the process of erosion is continued upon the deep surface of the cartilage. The process is not entirely one of destruction, for osteoblasts may lay down

Chronic infective arthritis. Ulcerative, ankylosing, and formative type in right knee-joint. Upper figure is lower end of femur, middle is upper end of tibia, and lower is patella. Femur shows thinning of entire joint cartilage with one small, rounded, thickened mass on internal condyle. On external condyle is an irregular area which articulated with the patella, to which it was joined by bony ankylosis. The upper end of the tibia shows ulceration of the articular cartilage. The patella shows that the articular cartilage has been replaced by bony ankylosis with the femur. Along the upper margins are newly formed spicules of bone (E. H. Nichols, in Keen's Surgery, vol. ii).

new bone on both the superficial and deep aspects of the articular cartilage. It is in the spine that the bony formation is seen to best advantage, and bony anchylosis of the articular processes may convert it into a solid, rigid column.

One of the characteristics of the disease is the involvement of the periarticular soft parts, to which some of the general swelling is due. Careful analysis of the symptoms will often reveal distinct evidence of fibrositis around the joints, which clears up readily under protein injections. In time the ligaments become softened and absorbed, a change which materially contributes to the deformities which form so distressing a feature of the end picture of the disease.

Osteo-arthritis

Osteo-arthritis in its well-developed form is so sharply demarcated from chronic infective arthritis that to include the two under the same heading is quite unjustifiable. In many cases, however, the destruction is by no means so marked. This group corresponds to the degenerative arthritis of Nichols. It merits the name arthritis deformans quite as much as the preceding group, but as the most striking changes are those in the bones the term osteo-arthritis is an appropriate one.

The disease is one of middle and old age, being rarely seen in the young, and then only following trauma. It is commoner in females than in males. A notable exception to this statement is the hip joint, and here again the element of trauma in the etiology is probably of great importance, as that factor is to be looked for in men rather than in women.

The onset is slow and insidious, and is not accompanied by those symptoms of toxic absorption which have already been noted in chronic infective arthritis. Fewer joints are involved than in the infective variety, and quite often the disease may be confined to one of the large joints. When the hip alone is singled out the disease is called *Morbus coxæ senilis*. The joints of the hands and feet are perhaps the most frequently affected, although the large joints, especially the hip, knee, and shoulder are often involved.

The appearance in the hand is highly characteristic. The knuckles are swollen into veritable knobs, and the distal phalanges are greatly enlarged, but the intervening proximal phalanges are often almost entirely spared. On the sides of the distal phalanges at the terminal phalangeal joints little bony outgrowths may appear. These are known as *Heberden's nodes*. Ulnar deviation of the hand is a characteristic deformity.

True anchylosis does not occur, as the pathology of the disease does not lend itself to such a complication, but there may be great limitation of movement owing to the formation of bony outgrowths around the joint. Occasionally, especially in the large joints, there may be undue looseness and mobility owing to absorption of the bone.

Etiology.—The nature and cause of osteo-arthritis are much more obscure than those of chronic infective arthritis. Its real nature

is quite unknown. It appears to be a degenerative rather than an inflammatory process, so that the term arthritis may be somewhat misleading. The usual list—cold, exposure, disorders of metabolism—is given in the text-books. One cause really does appear to play an important rôle in a number of instances, and that is trauma, especially in the case of the hip joint following a fall on the trochanter. These cases pursue a more rapid course than usual.

There is no good evidence that the disease is due to bacterial infection. It has been suggested, and not without reason, that there may be a relationship between arteriosclerosis and osteo-arthritis. The disease usually occurs after middle age, and in many cases the arteries show marked endarteritis obliterans. It must be admitted, however, that arterial degeneration and advancing years go together; the stealthy hours, as Clifford Allbutt puts it, are constantly stealing away qualities of tissue and quantities of energy. Whether or not the articular surfaces share in these depredations we are really not in a position to say.

Morbid Anatomy.—The disease differs from chronic infective arthritis in that it commences in the articular cartilage with secondary involvement of the bone instead of primarily attacking the synovial

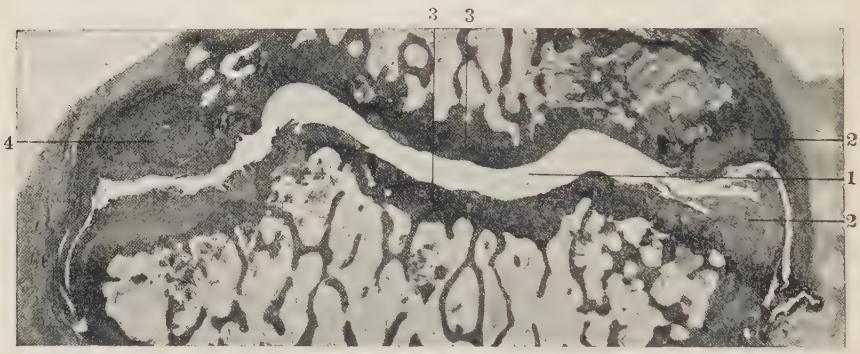


Fig. 336.—Osteo-arthritis. Photomicrograph of the phalangeal joint and adjacent phalanges. The line of the joint cavity is very irregular, 1; the cartilage has been almost entirely destroyed and shows only at the margins of the joint, 2; the articular surface of the phalanges where the cartilage has been destroyed is eburnated, 3. There has been a new growth of bone at the periphery of the joint (beginning Heberden's node), 4. The erosion of cartilage and eburnation, in this case, affects both sides of the joint articular facets. (E. H. Nichols in Keen's Surgery.)

membrane. At a later stage, it is true, both the synovial membrane and the periarticular tissues are implicated, but it is primarily a bone disease, a true osteo-arthritis.

The Cartilage.—Under the influence of the unknown causal agent the cartilage begins to degenerate. The smooth surface becomes roughened, being carried up here and there by delicate fibrils which give it the appearance of the pile of velvet.

The explanation of this appearance is seen in microscopic sections. The ordinary arrangement of the cartilage cells becomes altered,

and they form columns running at right angles to the surface, and separated by a matrix which degenerates and becomes converted into fine fibrillæ running in the same direction. The cartilage cells enlarge, causing distension of their capsules, and the latter burst, discharging the cells into the joint cavity. The intervening fibrillar matrix gives the appearance of the delicate tufts already observed by the naked eye. The matrix in turn softens, and so becomes worn down by the movement of the opposing articular surfaces.

In course of time the entire thickness of the cartilage becomes eaten away, and the underlying bone is exposed. The process occurs irregularly, and as a groove forms on one articular surface a corresponding thickening, at first cartilaginous and later bony, is formed on the opposing surface. In this way a parallel series of ridges and furrows may be developed, such as are seen in no other disease. These are found in hinge joints such as the elbow and knee. They are naturally absent in joints with a ball and socket action.

The changes so far described occur in that portion of the cartilage which Timbrell Fisher calls the central articular area (see page 751). In the lateral part of the articular surface the changes are quite different owing to the better nutritional arrangement and consequently the greater power of proliferation to which reference has already been made. In this area there is a marked proliferation of cartilage which, according to Fisher, always succeeds the degenerative changes in the central area, giving rise to a series of excrescences or ecchondroses, sometimes likened with justice to the drippings from a tallow candle. These may form a ring around

Fig. 337.—Osteo-arthritis. Extreme erosion of the head of the femur, with polishing and exostosis formation. (MacCallum.)

the edge, producing an appearance of lipping. This new cartilage is largely formed by the synovial perichondrium. Many of these chondrophytes become ossified and converted into osteophytes, the surface of which ultimately degenerates and the subjacent bone becomes "eburnated." Fisher points out that the new formations actually extend the articular surface in many cases, and may be regarded to a certain extent as compensatory. The under surface of the osteophytes may be supported by buttresses which resemble those in the roof of a Gothic cathedral, and are required owing to the extremely open nature of the osteophytes which they support. Some of the processes may become detached and form foreign bodies in the joint.

The Bone.—The most characteristic changes are to be observed in the bone. As the cartilage is worn away the underlying bone is

Fig. 338.—Osteo-arthritis of knee, showing osteophytic outgrowths.

exposed. This bone becomes condensed, extremely hard, brilliantly polished, and comes to resemble ivory or porcelain, a process known as *eburnation*. This change is usually attributed to the attrition of the opposing articular surface, but it is difficult to accept this explanation as entirely sufficient, for it is seen in no other joint disease. The chronic irritant responsible for the disease may play a part equal in importance to that of the mechanical friction. It is difficult to

explain otherwise the occasional occurrence of this change in such bones as those of the carpus, where the process of attrition is at a minimum. The polished surface is sometimes pitted as if worm-eaten. This is due to exposure of the Haversian canals of the underlying bone. The remarkable series of ridges and furrows already described may break the smooth surface of the bone.

The bone deep to the condensed layer undergoes a slow process of rarefaction and absorption. This is well seen in the hip joint, where the greater part of the head and neck of the femur may become absorbed. Irregular new bone formation may go on at the same time at the margin, so that the atrophied head of the bone is surrounded by excrescences which give it a mushroon-like appearance. The acetabulum undergoes similar changes so that it becomes enlarged

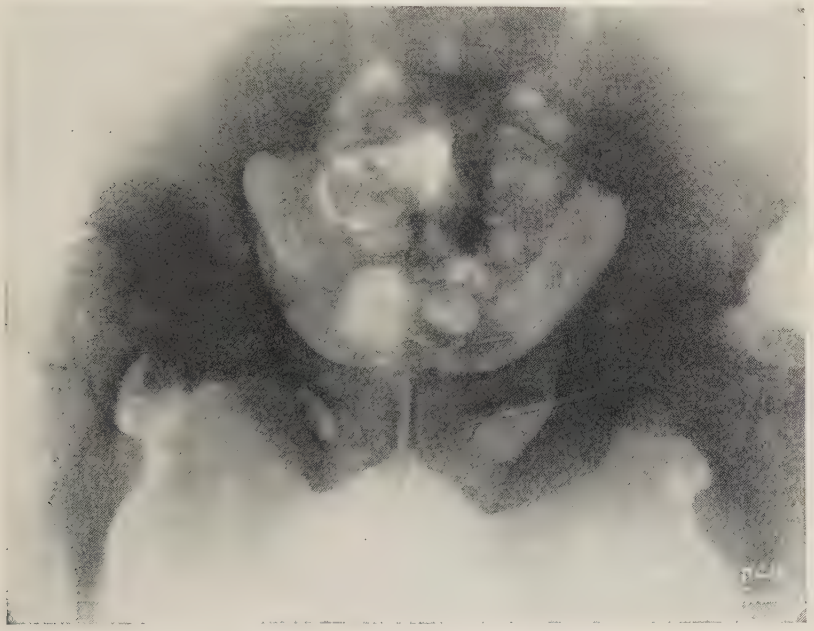


FIG. 339.—Osteo-arthritis of the hip. Proliferative changes well marked.

in an upward and backward direction, and surrounded by osteophytes. The presence of these periarticular processes greatly interferes with the action of the joint.

The Synovial Membrane.—Although the disease process is not primary in the synovial membrane, sooner or later that structure undergoes characteristic changes. It becomes thickened, shaggy, and a series of fringes and tags hang from the surface of the capsule into the interior of the joint. In many of these tags cartilaginous change occurs, and they may become detached, giving rise to "joint mice."

The *synovial fluid* may be increased to a moderate extent in the early stages of the disease, and is usually somewhat milky owing to the discharge into it of the cartilage cells. Later the effusion becomes absorbed.

The Ligaments.—The gradual process of dissolution which has already been described as occuring in the cartilage and bone involves the ligaments also. There is no violent destruction, but the ligaments simply melt away as if under the action of some solvent, causing great disorganization of the joint, with, in some cases, spontaneous dislocation. The lateral ligaments of the knee and even the crucial ligaments may entirely disappear.

Neighboring tendons may share a similar fate. The best examples are seen in the shoulder joint where the intraarticular portion of the long tendon of the biceps and the tendons of the scapular muscles attached to the tuberosities of the humerus may become destroyed.

The Periarticular Tissues.—These often show changes which it is difficult to explain, and which would rather be expected in chronic infective arthritis. Wasting of the surrounding muscles is often extreme, and suggests an additional factor besides disuse. An edema of the subcutaneous tissues may extend for some distance beyond the joint, and the overlying skin is pale, tight, and shiny. When the edema passes off the skin is thin and wrinkled like crinkled tissue paper.

Spondylitis Deformans.—Osteo-arthritis as it affects the spine, where it is known as spondylitis deformans, is deserving of separate mention. A certain amount of rigidity of the spine may accompany the ordinary form of osteo-arthritis. The term spondylitis deformans is confined to those cases in which there is marked disease of the spine with little or no implication of the peripheral joints. The disease is commoner in men, and it is possible that trauma may play some part in the etiology.

The cardinal factor is rigidity. The spinal column may be so stiff and straight as to suggest the term "poker back." Later in the disease the normal spinal curvatures may be lost, and the column is converted into a bow with its convexity backwards. The miserable patient becomes more and more bowed down, till ultimately the chin may rest upon the sternum and he is unable to look up. Anchylosis of the costo-vertebral joints results in such a fixation of the thorax with corresponding interference with respiration that any respiratory disease is apt to prove fatal.

Neuralgic pains, due probably to pressure on the nerves passing through the intervertebral foramina, are of frequent occurrence. These are principally felt around the thorax owing to pressure on the thoracic nerves, and down the back of the thigh from pressure on the great sciatic nerve. The corresponding muscles may be markedly atrophic.

Morbid Anatomy.—The changes are those which have just been studied, but there is one all-important exception to which the symp-

toms are due. There is anchylosis, complete and bony. The disease begins in the intervertebral cartilaginous discs, which gradually melt away. Osteophytic formation and lipping of the articular margins interfere with movement. It is, however, when the bodies of the vertebræ become fused together into one rigid mass that the real trouble begins. Moreover the ligaments share in the process. The anterior common ligaments may become converted into a rod of bone which binds many vertebræ firmly together. The ligamenta subflava and the interspinous ligaments may also become ossified. To that form in which the hip and shoulder joints are also prominently involved the name *spondylose rhizomelique* is applied.

A Comparison between the Two Forms of Chronic Arthritis

Chronic Infective Arthritis	Osteo-arthritis
A disease of early adult life.	A disease of over middle age.
Symptoms of constitutional disease, suggesting infection.	None.
Synovial membrane and periarticular tissues chiefly affected.	Cartilage and bone chiefly affected.
May be acute in onset and run a rapid course.	Essentially chronic.
Hip joint rarely affected.	Hip joint often affected.
Effusion into the joint common.	Effusion into the joint rare.
Fibrous adhesions between articular surfaces.	Any rigidity due to bony outgrowths around joint.
No Heberden's nodes.	Heberden's nodes may be present.
Many joints involved, usually in a symmetrical manner.	Often only one joint affected; usually symmetrical when multiple.
No relation to previous injury or disease of joint.	Previous injury or disease frequent.

CHARCOT'S DISEASE OF JOINTS

It was in 1868 that Charcot first described the peculiar disorganization of joints which may occur in the course of locomotor ataxia. Since that time little has been added to our knowledge of its essential nature. It is usually regarded as being due to interference with the trophic nerve supply to the joint, but this seems by no means a satisfactory explanation. Why should the disease in some cases appear with such dramatic suddenness, and why should the condition be usually confined to only one joint? A trophic neurosis hardly seems to account for such phenomena. It has also been suggested by Strumpell that it is a purely syphilitic lesion. The pathology of syphilis, however, presents no analogy to this condition. Moreover, identical lesions are found in the arthropathy of syringomyelia, which is certainly not a syphilitic disease. Charcot's disease must, therefore, be still regarded as an unsolved problem.

The joint affection may occur at any stage of tabes. Not infrequently it is quite an early symptom, and occasionally it may be the first indication of the disease. I have seen a patient with well advanced Charcot disease of the ankle and commencing disease of the elbow in whom there was not a single sign of tabes. Both the blood and the

spinal fluid gave a four plus Wassermann reaction. In about 80 per cent of cases the joint involved is in the lower limb, owing to the site of the cord lesion being usually in the lumbar region. The knee, the

Fig. 340.—Charcot's disease of the ankle joint. Natural position of the foot without the joint being forcibly opened. The extraordinary destruction of bone is very evident.

hip, and the ankle are the principal sufferers, but the joints of the foot or of the upper limb may be attacked. As a rule only one joint is involved.

The onset is usually slow, and the condition is mistaken for osteo-arthritis, with which it has many features in common. There is gradual enlargement of the joint, due in part to swelling of the soft tissues, accompanied by increasing weakness and disability, until finally the joint is completely disorganized and flail-like, and can be moved freely in all directions. Complete absence of pain is the most characteristic and remarkable symptom, and to be able to move about a profoundly diseased knee joint in all directions without any discomfort to the patient is apt to be somewhat startling to the examiner.

FIG. 341.—Charcot's disease of the ankle.

Not infrequently the onset is much more rapid, and the joint be-becomes painlessly distended with fluid within a couple of days. Destructive processes proceed with great rapidity, and the ends of the bones melt away like snow before the sun.

Morbid Anatomy.—The joint changes vary with the acuteness of the course. In the more chronic forms there is, at least at first, a distinct resemblance to osteo-arthritis. There are the same wearing

away of the cartilage, exposure and destruction of the bone, and thickening of the synovial membrane which is provided with numerous fringes and tufts. In some cases there may even be new formation of bone, as evidenced by the presence of osteophytes and lipping of the articular surface.

In the acute cases and in the later stages of the chronic cases the process of dissolution and disintegration reigns supreme. In the case figured in the text (Fig. 340) the interior of the ankle joint presented an extraordinary appearance of disintegration, as if some powerful solvent had been poured into it which had eaten away all the solid structures. A great yawning cavity filled with chocolate-colored fluid contained a number of fragments of bone, including the external malleolus. Into this cavity projected a ragged stump representing the lower end of the tibia. The greater part of the astragalus had vanished, the only portion which was capable of any function being the head. Nowhere was there any evidence of new bone formation. Nothing further from the picture characteristic of osteo-arthritis could be imagined.

Arthropathy in Syringomyelia.—An arthropathy which might well be called Charcot's disease occurs in syringomyelia. As the gliosis of this nervous disease involves the upper segments of the cord, the joints affected in about 80 per cent of cases are those of the upper limb. The anatomical changes are the same as those of tabetic arthropathy, but suppuration is liable to occur owing to infection from the burns and trophic sores which are so commonly present on the hands.

HEMOPHILIC JOINT

In hemophilia, in addition to hemorrhages from the skin and mucous membranes, there may be hemorrhage into one of the large joints. Such hemorrhage may be the result of an injury or it may be spontaneous. The joints most frequently affected are the knee, elbow, and ankle. If this hemorrhage is repeated at intervals the joint becomes swollen and stiff.

Morbid Anatomy.—The appearance when the joint is opened will naturally depend upon the amount of time which has elapsed since the last hemorrhage. It may contain old or recent clot. Apart from this, however, an interesting change will be observed in many cases in the articular elements, a change which closely resembles that seen in osteo-arthritis. The cartilage is fibrillated and eroded, the underlying bone is exposed, the articular edge is surrounded by osteophytes, and the blood-stained synovial membrane is thickened and presents numerous villi.

The resemblance of the joint lesions in hemophilia to those of osteo-arthritis are of great interest. If the presence of a chronic irritant in a joint in the former disease can induce such a series of changes, it encourages a search in the latter for some similar etiological factor.

Pulmonary Hypertrophic Osteo-arthropathy.—This peculiar condition, affecting both the bones and joints, was first described by Marie in 1890. It occurs as a complication of chronic pulmonary disease,

notably tuberculosis, bronchiectasis, and empyema. A somewhat similar clubbing of the fingers is met with in chronic heart disease, especially of the congenital variety with marked cyanosis. Indeed it appears probable that the two conditions are really indentical, simple clubbing of the fingers being merely an early stage of secondary hypertrophic osteo-arthropathy.

The hands and feet are enlarged, so that the condition must be distinguished from acromegaly, but the distinctive feature is the great swelling of the terminal phalanges of the fingers, and the thickened and curved nails. The lower ends of the bones of the forearm and leg are usually enlarged.

The chief change is a periosteal thickening of the bone, accompanied by thickening of the soft parts. The articular cartilage shows some erosion. There may be a moderate amount of effusion into the joint.

Two factors appear to play a part in the etiology. (1) The absorption of toxins from a septic focus in the lung or pleural cavity is undoubtedly the most important cause of the chronic periostitis. (2) Insufficient aeration of the blood seems to be capable of bringing about somewhat similar changes, for this is the only factor apparent in the cardiac cases, although in these cases congestion must also be taken into account.

GONORRHEAL ARTHRITIS

One of the common and important causes of arthritis is gonorrhea. The joint involvement is most frequent at the end of the third week or during the period of decline, but it may occur many months after the acute attack when only a slight gleet remains to tell the tale.

The gonorrhea need not be urethral in type. A gonorrheal conjunctivitis or vulvo-vaginitis may be followed by arthritis. It is well to note also that not all cases of arthritis associated with a urethral discharge are gonorrheal in nature, as other organisms than the gonococcus may reach the joints from the urethra.

The process is a metastatic one, and the organism reaches the joint by the blood stream. Owing to technical difficulties it is often impossible to isolate the gonococcus from the exudate in the joint. In long-standing cases this may be due to the organism having died out.

Although gonorrheal arthritis is a common disease, the percentage of cases is not high, ranging from 2 to 5 per cent. In some people there appears to be a special susceptibility so that each time they get an attack of gonorrhea they develop arthritis. We have already seen that the same holds true for gonorrheal orchitis. The disease is much commoner in males than females.

As a rule only a few joints are affected, and these are usually of the large variety. The knee is the most frequent sufferer, being involved in about two-thirds of the cases. Then come the ankle, fingers, hip, wrist, shoulder, and elbow. Some joints are attacked which are almost always exempt in rheumatic fever, a valuable point in differential diagnosis. Such are the temporo-maxillary, the sterno-clavicular,

and the sacro-iliac. The plantar fascia shares in the inflammation, and through softening and yielding a condition of flat-foot develops. The painful heel of gonorrhea is due to a periostitis of the os calcis.

As Osler remarks, variability and obstinacy are the two most distinguishing features of the disease. The pathological condition in the joints varies widely in different cases. This variation depends largely upon the virulence of the gonococcus when it reaches the joint. If the gonococcus is transferred from the urethra to the joints at the height of an acute attack, a correspondingly acute attack of arthritis will result, involving two or three of the large joints, and the condition may be mistaken for acute rheumatic fever. If, on the other hand, the arthritis arises during the course of a long-standing gleet, the gonococcus will be greatly attenuated, and will act upon the joint as a mild chronic irritant, causing a condition which may readily be mistaken for tuberculosis. Gonorrheal arthritis affords a beautiful example of the varying reactions of the tissues to an irritant which varies in strength, reactions which have already been studied in Chapter II. The following conditions may be encountered.

1. If the irritant is very mild the inflammation may only manifest itself by articular pains, without any of the physical signs of inflammation such as heat and redness. This is inflammation with *resolution*.

2. Another reaction to a mild infection is *hydarthrosis*. The onset as a rule is gradual, but may be acute. The joint becomes distended with fluid, but there is little pain or other sign of inflammation. The pathology is a subacute synovitis, which in time clears up completely. As a rule only one joint is affected.

3. When the irritant is more severe an acute arthritis may result. One or more of the large joints becomes swollen, red, hot, and extremely painful. In addition to the local signs there are fever and other constitutional disturbances. The effusion into the joint is turbid, but usually only moderate in amount. Much of the swelling is due to edema of the periarticular tissues. The lesion is an *acute synovitis*, but without tissue destruction, so that it also ends in resolution.

4. A very severe infection may produce a *pyarthrosis*, the joint becoming distended with pus. Fortunately this is a rare occurrence. This is inflammation with tissue death, and of course resolution is impossible, repair with fibrosis being all that can be hoped for.

5. Finally, a low-grade infection may cause a *chronic and persistent arthritis*, and this is the commonest of all the forms of gonorrheal rheumatism. The onset is gradual. At first a number of joints are involved, but most of these soon clear up, and one or two of the large joints are left to bear the brunt of the attack. There is considerable swelling, but this is due rather to the periarticular edema than to effusion into the joint, which is seldom marked. There may be some pain and local heat. Even after a prolonged course resolution may be complete. All too frequently, however, fibrous adhesions form, leading to permanent stiffness of the joint.

SYPHILIS OF THE JOINTS

The frequency with which syphilis attacks the joints is still a matter on which there are considerable differences of opinion. It is true that it is usually considered a rare disease. But it is equally true that, as the local signs are in no way characteristic, many cases may be mistaken for other joint diseases, the more acute forms for subacute rheumatism, the more chronic for tuberculosis or chronic arthritis.

A recent enquiry by Clark on the incidence of joint syphilis in the Panama Canal Zone throws valuable light on the subject. In a series of 1100 consecutive autopsies in which the joints were examined, joint lesions were found in 172 cases, and of these 96 were due to syphilis. These figures would go far to prove that syphilis of the joints is of much greater frequency than has been considered hitherto.

The disease may involve the joints in either the acquired or the congenital form, and in acquired syphilis joint disease may occur in the secondary or the tertiary stage.

Secondary Syphilis.—Minor forms of joint lesions are common in the early stages of the infection, due probably to the spirochetes producing transient changes in the synovial membrane analogous to the rashes in the skin and the early lesions of the mucous membranes. There may only be joint pains, worse at night, and with no physical signs observable in the joints.

In other cases there is more definite evidence of *synovitis* in the shape of swelling and a moderate degree of effusion into the joint. The knees are most frequently affected, and the condition is often bilateral. The diagnosis, as in all other forms of syphilitic arthritis, cannot be made from the local examination alone; the history, the evidences of syphilis, and the Wassermann reaction must all be taken into consideration. The synovial membrane would probably show a certain amount of swelling, but autopsy evidence on the subject is naturally almost completely lacking.

Later in this stage there may be a *hydarthrosis* in which the joint fills up with fluid. The condition is very intractable to treatment. A peculiar feature about syphilitic effusions is their remarkable and irregular variability. The effusion may almost disappear, then without apparent reason it may return and remain constant for a considerable time, only to make another mysterious spurt.

Tertiary Syphilis.—The joint lesions of late syphilis are those which would be anticipated from a consideration of the general pathology of the disease. Gummatous formation or diffuse inflammatory infiltration involves the synovial membrane as a rule, more rarely the articular ends of the bones.

In the *synovial form* there is an abundant gummatous formation in the synovial membrane, which may become a half or even one inch in thickness, and to an even greater extent in the subsynovial connective tissue and in the periarticular soft parts. The result is that, even although effusion is as a rule very moderate in amount, there is a

marked chronic swelling of the joint which so closely resembles that of tuberculosis that the French have given the name of "syphilitic white swelling" to the condition. If such a joint be opened it will be found that the irregular and nodular thickening of the membrane is very different from the tubercle-studded surface so often seen in tuberculosis. In addition to the synovial involvement there may be, as is but natural, gummatous erosion of the bone and cartilage, so that the condition is sometimes known as syphilitic osteo-chondro-arthritis. The disease is not particularly common, for Fournier only found 30 cases in 5000 syphilitics.

In the *osseous form* the disease begins in the articular ends of the bones, which become enlarged, and spreads later to the synovial membrane. Nocturnal bone pains are therefore a prominent symptom.

It will thus be seen that there are three principal forms of joint disease in acquired syphilis: (1) the simple synovitis of the secondary stage, (2) gummatous synovitis, and (3) gummatous osteitis.

Congenital Syphilis.—We may distinguish two main forms of joint disease in congenital syphilis.

1. *Synovitis.*—This may take the form either of a simple effusion or a gummatous synovitis. It occurs in older children and young adults. The knee joint is usually affected, and the condition is often bilateral. In the simple synovitis the effusion may be very considerable. It is but natural that the disease should often be mistaken for tuberculosis.

2. *Syphilitic Epiphysitis of Infants.*—The neighboring joints may be involved in this form of bone disease, which has already been described on page 715. The epiphysis is enlarged, the joint swollen, and there may be tenderness and pain. Owing to the frequent separation of the epiphysis the condition is sometimes called syphilitic pseudo-paralysis.

Other rare forms of joint disease in congenital syphilis have been described by Fournier, Bowlby, and others.

LOOSE BODIES IN JOINTS

Loose bodies in joints are of common occurrence, but there is still great diversity of opinion as to their nature and origin. The variety of the structures which may form these bodies adds to the difficulty of the subject.

The loose bodies may be divided into two great groups: (1) fibrinous loose bodies; (2) loose bodies composed of organized connective tissue. The latter may be fibrous, fatty, or cartilaginous. All varieties of loose bodies are commoner in diseased joints, especially in tuberculosis, osteo-arthritis, and Charcot's disease. What may be called the classical loose body, that composed of cartilage, is found in joints which are otherwise healthy. All of the bodies are most common in the knee and elbow, although they also occur in other joints.

Fibrinous Loose Bodies.—In many joints the seat of tuberculosis or osteo-arthritis there may be found peculiar, small, rounded, or

elongated bodies resembling melon-seeds or rice-grains. They are usually numerous, sometimes indeed there may be hundreds present, but occasionally there is only one, in which case it may attain a considerable size. They are of moderate firmness, and often present a laminated structure similar to that of a grain of rice. Microscopically they display a vaguely fibrillar structure.

They are probably formed by a fibrinous change in the surface of the synovial membrane, but the exact mechanism is by no means clear. Once formed they may increase in size owing to deposition of fibrin from the fluid exudate which is always present. They

Fig. 342.—Rice and melon-seed bodies from tuberculous palmar ganglion. Many of the bodies show pedicles. (J. F. Binnie in Keen's Surgery.)

are also found in abundance in synovial sheaths and bursæ the seat of tuberculosis. The greatest number I have ever seen was in a case of tuberculous compound ganglion of the wrist in which the large synovial-lined cavity was simply packed with melon-seed bodies.

These fibrinous bodies impart a characteristic crackling sensation to the palpating finger. They do not give rise to the well-known symptoms due to impaction of a loose body in a joint.

Masses of fibrin may arise from blood effused into a joint. These, of course, are quite distinct from the melon-seed bodies.

Fibrous and Fatty Loose Bodies.—Under a variety of circumstances tags of fibrous tissue or fat may be formed, which tend to become more and more pedunculated, till finally they separate and form loose bodies.

As the result of an injury the synovial membrane may be torn, and the constant irritation induced by the movements of the joint sets up a condition of chronic inflammation, as the result of which a thickened and finally pedunculated tag is formed.

A much more important cause is the presence of tuberculosis or osteo-arthritis in the joint. In both of these diseases the synovial

membrane may present a fringed and villous appearance, and one or more of these fringes may give rise to loose bodies. In a given joint some of the bodies may be free, some still attached by slender pedicles, and yet others may appear as if they never could become free.

Arborescent lipoma is the name given to the exuberant fringing of the synovial membrane sometimes seen in chronic arthritis. It is very prone to give rise to the formation of loose bodies, and is of course in no sense a true lipoma.

Cartilaginous Loose Bodies.—This is the most interesting and important group of loose bodies, and it is these which give rise to the classical symptoms of loose body in a joint. They may be divided into three groups. (1) Osteophytes. (2) Traumatic fragments in otherwise normal joints. (3) Synovial chondromata. The osteophytes, it is true, owe their existence as separate loose bodies to trauma, but the special significance of trauma in the causation of the second group will become apparent when that group is considered.

1. *Osteophytic Loose Bodies.*—An osteo-arthritic joint frequently presents osteophytic outgrowths so prominent and pedunculated that it is little wonder that they become detached as the result of even a trifling injury. The chondro-osteophyte may be completely separated, or may remain attached to the joint margin by a slender pedicle.

When such a fragment is examined closely it will be found that the bone at the site of fracture is completely dead, and that the periphery consists of well-developed fibro-cartilage with comparatively few cells. It is seldom that more than two or three of such bodies are found in a joint, and often there is only one. There may be in addition several cartilaginous loose bodies derived from synovial fringes.

In the hypertrophic variety of Charcot's disease osteophytic formation may also give rise to loose bodies, sometimes of great size.

Reference may be made here to the presence of a tuberculous sequestrum in a joint, although it cannot be classed as an osteophyte. Necrosis with separation of a fragment of bone is not characteristic of tuberculosis, in which rarefaction and caries are the rule, but it may occasionally occur, especially at the articular end of the femur. The process is probably due to interference with the blood supply, which explains the wedge-like form of the sequestrum. Such a sequestrum may form an osseous loose body in the joint.

Similarly, in acute arthritis there may be separation of part or the whole of an epiphysis, which comes to lie loosely within the joint. These two varieties of loose body are only included here for the sake of academic completeness.

2. *Traumatic Fragments in Normal Joints.*—It is feared that this title is a question-begging one, for very different views have been held regarding this, the classical form, of loose body in a joint. The recent work of Timbrell Fisher, however, has demonstrated that the majority of these cases are not due to a process of "quiet necrosis"

gradually causing separation of a portion of the articular surface, as was suggested by Sir James Paget and others, but that the separation is due either to direct trauma or to muscular or ligamentous strain, either occasional or frequently repeated.

The general characteristics of such a loose body as outlined by Fisher are as follows. It occurs more frequently in males than females, and usually between the ages of 15 and 25. It is circular or oval in shape, about the size of an almond, and is plano-convex. The convex surface is smooth and has the typical appearance of articular cartilage, whereas the plane surface is roughened, although subsequent changes may smooth it down. Its commonest site is the knee, and then the elbow. In the case of the knee it is derived from the femur or patella, rarely from the tibia. It may be completely or incompletely detached, or may acquire a secondary adhesion to the synovial membrane. Its continual presence may lead to osteo-arthritic changes in the joint. It may undergo remarkable proliferative changes.

In recent cases the cells of the bony part of the fragment are alive. Were a quiet necrosis the cause of the separation the bone would be dead. The cartilage is hyaline articular cartilage, very different from the fibro-cartilage of the osteophytic loose body.

In some cases the loose body, after remaining in the joint for a considerable time, may show evidence of proliferation. Cartilage is laid down around the original body, sometimes in an irregular nodular manner, sometimes concentrically. In one case described and figured by Fisher the body was 2½ inches in diameter, and the surface was extremely irregular and coral-like.

3. *Synovial Chrondromata.*—Many years ago Kölliker showed that cartilage cells occur normally in the villous processes of the synovial membrane. It is but natural, therefore, that many loose bodies derived from synovial fringes should become converted into cartilage. It sometimes happens that these cells take on a true tumor growth, with the result that chondromata are formed.

Such chondromata may be single, but are frequently multiple. They may or may not be laminated. The number present may be remarkable. There is a specimen in the museum of St. Bartholomew's Hospital showing 415 of these bodies removed from the knee joint, and James Berry has recorded a similar case in which no fewer than 1047 cartilaginous bodies were found in the knee joint of a woman 22 years of age.

The surface of the synovial membrane may be studded with these small cartilaginous nodules. Usually discrete, they may when compressed become caked into large masses. Microscopically they consist of hyaline cartilage.

CYSTS CONNECTED WITH JOINTS

There are two main varieties of such cysts. (1) The cyst may be due to the distension of a bursal sac which normally communicates

with the joint. (2) The cyst may be formed by a pouch-like protrusion of synovial membrane through gaps in the capsular ligaments. These latter cysts were first described by Morrant Baker, and are known as Baker's cysts. Their mode of formation is similar to that of an aneurism. It is natural, therefore, that the two conditions which predispose to such cysts are increased in the pressure within the joint and some disease process which will weaken the parts. These conditions are found in tuberculosis and osteo-arthritis.

Fig. 343.—Baker's cyst which extended from the knee joint to the tendo Achilles.

A Baker's cyst is usually found in connection with the knee joint. One of its important characteristics is its tendency to track through the tissues and thus recede from the joint. In this way the cyst may become so far removed from the joint that its nature is not recognized, and it may be opened on the assumption that it is a chronic abscess, the almost certain result being an infection of the joint. The distance to which these cysts may extend is sometimes phenomenal. I have dissected out one such cyst as far as the tendo Achilles (Fig. 343). Throughout most of its course it was very adherent to the surrounding tissues.

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CHAPTER XXXVI

THE MUSCLES, TENDONS, AND BURSÆ

THE MUSCLES

A voluntary muscle consists not only of muscle fibers but also of a fairly abundant interstitial connective tissue. It is this interstitial tissue which is involved in many of the pathological conditions affecting muscles, such as inflammations and neoplasms.

Atrophy.—Atrophy of a muscle may be due to three main causes: (1) disuse, (2) joint disease, and (3) nerve involvement.

1. Atrophy from disuse occurs whenever a muscle is not kept in full functional activity. Eventually almost all the contractile substance may disappear, and the muscle sheath becomes filled with fibrous and adipose tissue. There is no true reaction of degeneration.

2. Atrophy is a very constant accompaniment of joint disease, but frequently it is greater in degree than can be accounted for by mere disuse. It may be, as first suggested by Paget, that impressions from the diseased joint pass up to the nerve cells in the anterior horn of the cord and there induce changes which give rise to what is really a neuropathic atrophy.

3. Atrophy of muscle will follow either interference with the motor nerve (probably owing to it's containing trophic fibers), or disease of the motor cells in the anterior horn. Of such disease the best examples are acute anterior poliomyelitis and progressive muscular atrophy. In the earlier stages the muscle shows the characteristic reaction of degeneration. Later it becomes largely replaced by connective tissue and fat.

Ischemic atrophy or Volkmann's contracture is an obscure condition occurring in young people, affecting principally the muscles of the forearm, and due to interference with the blood supply from the use of tight splints or a tourniquet, and probably in part to pressure on the nerves. Within a few hours the muscles lose their power, and become swollen and very hard. Pain is usually present—due, perhaps, to an accompanying neuritis—but if absent the gravity of the condition may not be realized. Contracture of the fingers is an early sign. The muscles may show the reaction of degeneration. The contracture is permanent, varying in degree with the duration of the ischemia.

Injury.—A muscle or a tendon may be injured by a direct blow, but rupture is frequently due to indirect violence, such as the sudden muscular exertion needed to regain the balance. Rupture commonly occurs at the junction between the muscle and its tendon. When rupture follows upon a comparatively trivial effort it may be due to the

sudden contraction of the opposing muscles occurring before the affected muscle has had time to contract fully, as in the classical instance of a professional athlete who ruptured his biceps whilst sitting at table and endeavoring to catch a falling glass.

Blood is poured into the gap, and union takes place by the formation of fibrous tissue as described on page 86. No new muscle fibers are formed. In the case of a ruptured tendon, however, new tendon may bridge the gap if it is not too wide.

Myositis.—Inflammation of muscle affects primarily the interstitial connective tissue. The muscle fibers are involved only secondarily, and they manifest degenerative rather than inflammatory changes. At no time a common condition, it may be due, (1) to the spread of infection from a neighboring focus such as an inflamed appendix, an empyema, an infected wound, and the like, or (2) to metastatic infection by the blood stream, especially in pyemia, typhoid fever, and gonorrhea.

The inflammation may be of any degree of intensity. There may be hyperemia and edema, fibrin formation, suppuration with abundant pus formation, or finally extensive gangrene and destruction. The last possibility is most likely to occur when anerobic organisms are present, especially when associated with much laceration of the tissues. It was only too common, therefore, in wounds of the muscles in the recent war.

The appearance of the affected muscle depends on the severity of the inflammation. At first it is red, swollen and sodden. Later it becomes of an unhealthy grey color, opaque, streaked with brown or yellow, with here and there areas of hemorrhage. Losing its normal firmness it becomes soft and friable, and if suppuration supervenes numerous pockets of pus are formed, and the pus may spread along the fascial planes. In the most severe forms, especially those due to anerobes, the muscle becomes converted into a sloughing mass of greenish-black putrid material, which breaks down into a most evil-smelling dirty fluid.

In the milder cases resolution may occur. When the change has gone on to tissue death, healing must be accompanied by more or less extensive fibrosis. The abscess cavities may be shut off by granulation tissue, the contents become inspissated, and eventually lime salts may be deposited.

Acute Polymyositis.—This rare and obscure condition is one in which there is a severe non-suppurative inflammation of many muscles. The onset is usually gradual, with lassitude and pains in the muscles suggesting trichiniasis, but as a rule little or no fever. The muscles chiefly affected are those of the tongue, the back, and the limbs. The pain becomes so acute that the patient is unable to move in bed. The muscles are swollen, hard, and extremely tender. Death may occur from paralysis of the respiratory muscles with a resulting pneumonia. After a period of many weeks recovery may set in. The affected muscles are brownish-red, with areas of liquifaction, the fibers being

degenerated and separated by round celled infiltration. A characteristic feature is the presence of erythematous or urticarial patches on the skin, so that the disease has been called dermatomyositis. The condition is supposed to be due to an intestinal toxemia, but the evidence for this is not sufficient. It is probably a non-pyogenic infection of unknown nature.

Myositis Ossificans.—Although this condition is not really an inflammation it may be considered in this place. Bone may be formed in muscle in two classes of cases: (1) progressive myositis ossificans and (2) traumatic myositis ossificans.

1. *Progressive myositis ossificans* is a disease entirely obscure in its nature and universally fatal in its outcome. Commencing usually in childhood, it is often ushered in by an acute attack of pain associated

FIG. 344.—General myositis ossificans affecting the muscles of the back.

with doughy circumscribed swellings in one or more groups of muscles, especially those of the back and neck. The further progress of the disease is by fits and starts, periods of remission being followed by aggravation of the symptoms. The affected areas gradually become calcified and converted into bony plates, until the body becomes enveloped in a rigid cuirass which renders all movement impossible, the pitiable condition being terminated by some pulmonary complication.

In one case which I had an opportunity of studying, and which has since been published by A. P. MacKinnon, the appearance of the back suggested the ridges on a relief map. Great masses of bone could be felt in the latissimus dorsi on both sides, in the deltoid, the brachialis anticus, and the triceps; a kind of poker passed from the mid-dorsal region to the sacrum, joining the spinous processes, and a bony band, an inch and a half wide, extended on each side from the os pubis to the upper part of the femur along the line of the upper margin of the adductor magnus; the rectus femoris and the muscles of the leg were also involved. Needless to say, the X-ray picture was bizarre in the extreme (Fig. 344). The patient was a young man of nineteen, and the disease made its appearance at the age of fifteen.

The condition appears to be at first an inflammation of the connective tissue of the muscle, and in the granulation tissue thus formed true ossification then occurs. It would almost appear that some congenital anomaly plays some part in the causation, for not only does the disease appear in early childhood, but other congenital defects such as microdactyly in the hand and absence of a phalanx of the great toe are very constantly present.

2. *Traumatic myositis ossificans* may occur as the result of repeated injury to a muscle, but occasionally it may follow a single trauma, such as the kick of a horse on the thigh. Repeated bruising of the adductor longus in cavalry soldiers may be followed by the development of a bony mass, the so-called rider's bone. The blow of the butt of a rifle on the pectoral muscle may give rise to a similar condition. Dislocation of the elbow may be accompanied by a bony formation in the brachialis anticus. If the new formation is attached to the bone there may be marked limitation of movement; if not the symptoms may be slight. The most probable explanation of the ossification is that some of the periosteal cells become detached and transplanted into the muscle, there to continue their normal function.

In addition to these well-defined varieties of ossification, there is quite often some bony formation at the attachments of muscles tendons, and in this way quite large spiculus of bone may be formed. Marked formation of bone may occur in the neighborhood of a Charcot joint. Indeed in one of our recent cases of this disease the bony masses in the muscles around the knee were so marked as almost to obscure the primary condition.

Fibrositis of Muscle.—There is a group of conditions in which the principal symptom is sudden and severe pain when a muscle is contracted. Some of the best-known examples are lumbago, affecting the muscles of the lower part of the back; stiff-neck, affecting the sternomastoid; and pleurodynia, affecting the intercostal muscles. It is to this class of case that the vague and unsatisfactory term of muscular rheumatism used to be applied.

There appears to be a subacute or chronic inflammation of the connective tissue of the muscle involving the nerve endings. The

inflammation may spread to the fascia, the periosteum, or the fibrous sheath of the nerves.

Tuberculosis of Muscle.—Tuberculous disease of muscle may occur in two forms. (1) It may be due to extension from a neighboring focus in bone, glands, or pleura. (2) It may be primary, that is to say it may be metastatic due to blood spread from some preexisting distant focus. The latter form is very rare, whilst the former frequently occurs from disease of the vertebræ, the hip joint, or the lungs.

A tuberculoma is first formed in the muscle presenting the usual histological appearance. Caseation occurs with the formation of a cold abscess, which may appear at a great distance from the initial lesion. The behavior of such a tuberculous abscess has already been considered in Chapter V.

Syphilis of Muscle.—Syphilitic lesions of muscle may appear in the secondary or in the tertiary stage.

In the early secondary stage there may be muscular pains, worse at night, due to a mild fibrositis. At a later stage there may be a syphilitic contracture, the nature of which is not understood. An extreme degree of contracture develops in some muscles, especially in the biceps, although without any definite anatomical lesion.

In the tertiary stage there may be either a diffuse syphilitic myositis or the formation of gummata. In the diffuse form there is a hardening of the muscle due to proliferation of the connective tissue owing to the presence of the spirochetes. Recovery under specific treatment is prompt. A gumma forms a firm, elastic swelling in the substance of the muscle, with subsequent necrosis and fibrosis.

The muscles principally affected by these syphilitic manifestations are the sternomastoid, the tongue, the calf muscles, and the levator ani.

Tumors of Muscle.—All tumors of muscle are uncommon, and most are extremely rare. Those which do occur arise not from the muscle fibers but from the connective tissue. A tumor of muscle is freely movable, at least across the long axis of the muscle, when the muscle is at rest, but it becomes firmly fixed when the muscle is contracted. Gummata and other masses occurring in muscle behave, of course, in a similar manner. Although theoretically any connective tissue tumor may be met with in muscle, the only ones of importance are fibroma, angioma, sarcoma, and carcinoma.

Fibroma.—The only variety of fibroma which calls for special notice is that which occurs in the anterior abdominal wall, especially in the rectus abdominis, to which the name of desmoid tumor is given. It occurs in women in 90 per cent of cases, and usually in those who have borne children. These tumors are mildly fibrosarcomatous, for they tend to recur locally when removed, so that Paget called them "recurrent fibroids."

Angiomas, whilst not common, are of importance, for, although characterized by pulsation, a thrill, a murmur, and the youth of the patient, they may be mistaken for other forms of tumor with unpleas-

ant results. I once entered an operating room to find the place swimming with blood, the surgeon having mistaken an angioma of the popliteal space for a fatty tumor. The muscles of the calf were so infiltrated by the growth that the leg had to be amputated.

Sarcoma.—Primary sarcoma of muscle is rare. Secondary growths are distinctly common.

Carcinoma is of course always secondary, and is far from common. There is a specimen in the University of Manitoba Pathological Museum of a large epitheliomatous mass in the flexor muscles of the forearm, secondary, apparently, to an epithelioma of the lip, a remarkable site for a metastasis in a tumor which rarely sets up any distant metastases.

Trichiniasis.—The embryos of the trichina are carried from the bowel to the muscles, especially the flat muscles, by the blood stream. An embryo enters a muscle fiber, becomes curled up, dies, and is surrounded by a fibrous capsule. The nodule becomes calcified. The stage of invasion is marked by severe pain and swelling of the muscles, fever, and other constitutional symptoms. The blood shows a well-marked eosinophilia.

Hydatids.—Hydatid cysts of the muscles occur in less than 2 per cent of cases of hydatid disease. They may form tumors as large as a hen's egg. Calcification usually occurs, so that a hard calcareous mass is formed.

THE TENDONS

Tenosynovitis.—Inflammation affects the sheath of a tendon to a much greater extent than the tendon itself, so that the condition is known as tenosynovitis. The inflammation may be due to (1) trauma, (2) pyogenic infection, (3) gonorrhea, (4) tuberculosis, (5) syphilis, and (6) gout.

Traumatic tenosynovitis occurs in those in whom the tendons are subjected to excessive use, as in piano-players. Considering the comparative infrequency of the condition it is probable that some other factor, possibly toxic, comes into play.

As in the pleural cavity, the inflammation may be dry or moist. In the dry form a deposit of fibrin is laid down upon the tendon and the walls of the sheath, producing a most characteristic symptom of creaking or crepitation similar to the friction of dry pleurisy. The breaking down of the adhesions, which are so apt to form and which produce considerable disability, has made the reputation of many a bone-setter. When effusion occurs the crepitation naturally disappears, and an elongated swelling appears in the long axis of the tendons. The tendons most frequently affected are the extensors of the wrist and the thumb, the peroneal and extensor tendons of the ankle, and the tendo Achilles.

Suppurative tenosynovitis is the result of the spread of infection in the neighborhood. The most frequent cause is a whitlow of the

fingers. As the tendon sheaths of the thumb and little finger are continuations of the flexor sheath in the forearm, infection of these digits is more far-reaching in its consequences. Abundant granulation tissue is formed within the sheath, so that firm adhesions may result. When the inflammation is more severe the tendons, which are very poorly supplied with blood, may slough.

Gonorrheal tenosynovitis is usually a mild inflammation, but it may be severe. In the mild form there is serous effusion into the sheath, giving rise to an elongated swelling, or no effusion may occur, there being merely pain and disability. In the severe form the inflammation may be so acute as to go on to suppuration. Even in that case, however, the tendons rarely slough. The tendon sheaths principally affected are those of the wrist and the ankle.

Tuberculous Tenosynovitis.—Tuberculosis of the tendon sheaths closely resembles tuberculosis of joints. It may, therefore, be primary in the tendon sheath, or may be secondary to bone disease. As with tuberculous arthritis, there are two main forms; in the first there is a diffuse and abundant formation of granulation tissue, in the second there is hydrops with the production of melon-seed bodies.

The *fungous* variety is analogous to the tuberculous white swelling of joints. The synovial sheath is filled with soft pulpy granulation tissue studded with tubercles. This undergoes caseation, and may break down and liquefy. This form is usually due to extension from a neighboring bone focus.

The *hydrops* form is characterized by an abundant serous effusion into the sheath. A limited amount of tuberculous granulation tissue is formed, on the surface of which a layer of fibrin is deposited. Owing to the friction of the tendon much of this fibrin becomes detached and converted into the little rounded masses known as rice-bodies or melon-seed bodies, which give a very characteristic crepitant sensation when the swelling is palpated. This is the condition which used to be called a compound ganglion. The sheath may be packed full of the melon-seed bodies (Fig. 342).

The tendon sheaths most commonly involved are the common flexor sheath of the wrist and the peroneal and extensor sheaths at the ankle. At the wrist the swelling is hour-glass shaped, owing to the constriction of the annular ligament.

Syphilitic Tenosynovitis.—In the secondary stage of syphilis a mild tenosynovitis may develop. In the later stages gummata of the tendon sheaths may occur.

Gouty Tenosynovitis.—In gouty patients there may be deposits of urate of soda in the tendon sheath or beneath the synovial covering of the tendons. These may give rise to nodular masses which can be felt to move with the tendon, and which may cause a considerable amount of irritation.

Tumors of Tendon Sheath.—The ordinary tumors of connective tissue occasionally occur in the tendon sheaths, and are very liable to be mistaken for tuberculous disease. A lipoma arising from the syno-

vial membrane often follows the course of the tendons, and at the wrist may give rise to a branching tumor.

Special reference must be made to the giant-celled tumor which occurs at the wrist or at the attachment of the tendon to the phalanx. This forms a firm mass of no great size, and is composed mainly of multinucleated giant cells. The structure is the same as that of the giant-celled epulis. There may be numerous xanthoma cells filled with lipoid material which gives a foamy appearance to the cytoplasm. Although microscopic examination may lead to a diagnosis of giant-celled sarcoma, local removal is all that is required. The question as to whether or not these tumors should be regarded as sarcomata has already been discussed in Chapter XI.

Ganglion.—A ganglion is a cystic swelling occurring in connection with a tendon sheath, especially in the neighborhood of a joint. The three principal sites where they occur are the back of the wrist, the dorsum of the foot, and the outer aspect of the knee. Of these the wrist is by far the commonest position.

The size varies from that of a pea to that of a plum. On the wrist it is usually rather soft, becoming tense when the wrist is flexed. On the foot it is more hard and tense, and is apt to be mistaken for a tumor. At the knee it may be confused with a bursa or a synovial cyst.

The capsule consists of dense fibrous tissue continuous with the surrounding connective tissue and especially with the tendon sheath. There is no endothelial lining, so that the fibrous capsule is in contact with the contents. The latter are clear and jelly-like.

The mode of formation is by no means clear. It used to be thought that the ganglion arose as the result of the protrusion through the fibrous capsule of the synovial lining of the tendon sheath or the joint. In most cases, however, no communication can be found between the ganglion and the tendon sheath, and even where such a communication does occur it appears to be secondary rather than primary. It is more probable that the connective tissue of the sheath undergoes proliferation followed by mucoid degeneration with the formation of a number of small cysts which eventually fuse into one large cavity. The essential reason for these changes is unknown.

The condition formerly known as compound palmar ganglion is not a true ganglion, but a tuberculous inflammation of the tendon sheaths at the wrist.

THE BURSÆ

A bursa is a sac lined by synovial membrane and containing synovial fluid. Similar as it is in structure to a joint and a tendon sheath, it is equally similar in the diseases to which it is liable. Many bursæ are preexisting, but others, called adventitious bursæ, are developed as the result of friction. Most bursæ are closed sacs, but a few communicate with a joint cavity; that, for instance, between

the gastrocnemius and the semimembranosus is usually continuous with the knee joint.

The principal pathological condition affecting a bursa is inflammation. This may be due to trauma, to infection, or to tuberculosis.

Traumatic bursitis may be the result of a blow, such as a fall on the knee (prepatellar bursa), the elbow (olecranon bursa), or the shoulder (subacromial bursa). More frequently, however, it is due to chronic irritation, as seen in the "housemaid's knee" or the "student's elbow." A condition of hydrops develops, the bursa being distended with serous fluid, sometimes to an extreme degree.

When the condition is of long standing the wall may undergo great thickening, and becomes covered by fibrous ridges, septa, and

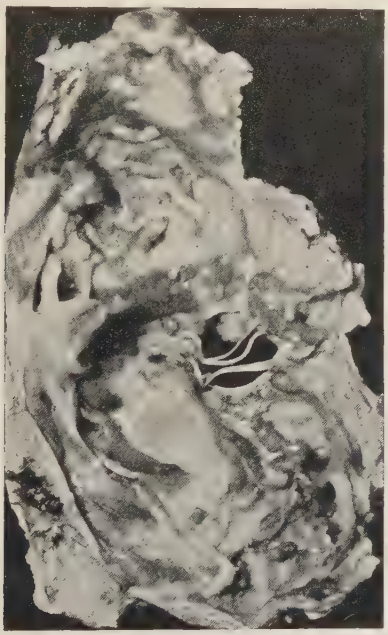

FIG. 345.—Bursa showing effects of chronic inflammation. The wall is covered by numerous tags, and fibrous bands traverse the cavity.

tags, so that the appearance somewhat resembles the interior of a joint the seat of chronic arthritis. The tags may become detached and form melon-seed bodies, which can be detected on palpation. Occasionally the thickening is so great that the cavity is almost obliterated, and the bursa becomes converted into a solid mass.

Infective bursitis is usually due to infection introduced by a perforating wound. Sometimes, however, it is the result of the extension of inflammation from the neighboring joint or bone. The olecranon and prepatellar bursæ are the most frequently affected, and become distended with pus, which may rupture the wall and pass for some distance along the limb.

Rheumatism and gonorrhea may give rise to inflammation of bursæ, especially in the subacromial bursa and in the bursa between the tendo Achilles and the os calcis.

Tuberculous bursitis is similar to tuberculous tenosynovitis. There may therefore be hydrops with melon-seed bodies, or an abundant formation of tuberculous granulation tissue with subsequent softening and liquefaction. The disease may be primary in the bursa or secondary to bone or joint tuberculosis. Any bursa may be affected, but special reference may be made to the subacromial bursa, owing to the difficulties of diagnosis which it may present unless the condition be kept in mind.

Tumors of bursæ are very rare. Sarcoma and giant-celled tumor are probably the most common. Gummata are of more frequent occurrence than true tumors.

CHAPTER XXXVII

EMPYEMA

The study of empyema has received an enormous stimulus during the last few years, partly because of its frequency as a complication of wounds of the chest during the war, but chiefly because of the extraordinary number of cases which developed in the course of the recent epidemics of measles, streptococcal pneumonia, and influenza. As a result of this study much fresh light has been thrown on the pathology of the condition, on the physiological mechanics of the thorax, and on methods of treatment.

Empyema is a collection of pus in the pleural cavity. The effusion may be purulent from the beginning, but more frequently it is at first serous or sero-fibrinous, becoming purulent later. The disease is commonest in the first two years of life, and the mortality is also highest during that period. About two-thirds of the patients are males.

Etiology.—The infection may reach the pleural cavity in the usual three ways: (1) by spread from neighboring organs; (2) by introduction from without; (3) by the blood stream.

1. *Spread from Neighboring Organs.*—The great majority of empyemas are due to the spread of infection from a pneumonic lung. Two great types of case must be distinguished: those which *follow* a lobar pneumonia and are caused by the pneumococcus, and those which *accompany* the streptococcal pneumonias which are so frequently associated with influenza, and less commonly with measles and the other exanthemata. The distinction is a fundamental one, because it has a most important bearing on the subject of treatment.

If the chest is opened in the early stages of a streptococcal case the result may be disastrous, for the pneumonia is still in full bloom, and in a patient whose vital capacity is already perilously low, who is cyanosed and suffering from marked air hunger, even a tiny opening in the chest wall may prove fatal. In pneumococcal empyema, on the other hand, the presence of pus is usually not detected until the pneumonia has subsided, so that the condition of affairs is similar to that obtained by delay of open drainage in streptococcal cases. A point in the differential diagnosis is that in pneumococcal empyema there is a marked leucocytosis, whereas in the streptococcal empyema of influenza the leucocyte count is normal or very slightly elevated, although in streptococcal cases following measles or abscess of the lung the count may be quite high.

How does the infection spread from the lung to the pleural cavity? In order that a purulent inflammation may develop it is necessary that

there be a fairly heavy infection of the pleural cavity. The view accepted until recently was that infection took place by contiguity, by the direct passage of the bacteria from the lung to the pleural cavity. To this idea there are several objections. If it were true there would seem to be little reason why empyema should not complicate every case of pneumonia. A diffuse suppuration seldom develops in the peritoneum from inflammation of a hollow viscus such as the appendix or stomach unless the wall of the viscus is perforated or so damaged as to

FIG. 346.—Subpleural abscess at upper part of lower lobe of lung which gave rise to empyema.

allow free access of bacteria to the peritoneal sac. The fibrinous exudate which invariably covers the surface of an inflamed lung serves as an efficient barrier to the spread of infection.

On theoretical grounds, therefore, we might suppose that many cases of empyema were due to discharge of infected material from the lung into the pleural sac, that is to say to rupture of a subpleural

abscess into the cavity. Now in the streptococcal empyemas which so frequently complicated the pneumonias in the recent influenza epidemic it was repeatedly found, as Moschcowitz in particular has emphasized, that the primary lesion was a subpleural abscess which had ruptured, and the more careful the search the more frequently was this condition discovered. It may be said, therefore, that the essential cause of streptococcal empyema is the perforation of a subpleural abscess. The same is true also of some cases of pneumococcal empyema, but whether this holds for the majority of cases it is difficult at present to say.

The perforation may be very small, in which case it will usually heal fairly readily. When larger, however, it remains open, and if, as is frequently the case, it communicates with a bronchus, a pleuro-pulmo-

Fig. 347.—Subpleural abscess at base of lung associated with empyema.

nary fistula will be established. This, being a constant source of fresh infection, is one of the most important causes for an empyema becoming chronic.

Although the lung is the most important neighboring organ from which infection may spread, there may be other primary sources of infection. An abscess in the mediastinum, an infective process in the chest wall, a subphrenic abscess, a liver abscess, suppuration in the gall bladder, and even inflammation of more distant organs may be followed by empyema. Wilensky mentions a case with repeated attacks of appendiceal colic in which a practically normal appendix was removed. A stormy course was marked by the development of a

fatal empyema, but no peritonitis nor subphrenic abscess was found at the autopsy.

2. *Introduction from Without.*—A perforating wound of the chest is liable to be followed by empyema. Although in civil practice this accident is not common, in the war it assumed a position of great importance.

3. *Blood Infection.*—In exceptional cases empyema may begin apparently as a primary condition. These cases are undoubtedly due to infection by the blood stream. More frequently the infection is carried from some recognized inflammatory focus elsewhere. Empyema may follow tonsillitis, appendicitis, acute otitis media, or puerperal sepsis. It may develop in the course of one of the acute infectious fevers, but probably in these cases pneumonia is an intermediate factor. An empyema may develop during a bacteremia, but in this case it acts as a fixation abscess, and the prognosis becomes distinctly more favorable.

Bacteriology.—The commanding part played by the pneumococcus and the streptococcus in the production of empyema has already been referred to. The statistics in the literature naturally vary considerably, depending upon the year in which they are compiled. During the months of the great influenza epidemic the streptococcus hemolyticus far out-distanced all competitors. During more normal periods the pneumococcus heads the list. In Wilensky's analysis of 574 cases the pneumococcus was present in 289, the streptococcus in 123, the staphylococcus in 86, the streptococcus mucosus in 10, the remaining cases being due to a large variety of other organisms. When the pus is found to be sterile the tubercle bacillus should always be suspected. Tuberculous empyema is comparatively infrequent, forming only 2 per cent of Wilensky's cases.

Morbid Anatomy.—An empyema, especially when secondary to a lung infection, is usually preceded by a slight exudation of serous fluid, which later becomes purulent. An abundant inflammatory exudate is deposited on the surface of the lung and on the parietal pleura, and pus is poured into the intervening space. So massive is this purulent exudate that there is a tremendous loss of nitrogen in the body, a point of considerable importance in the dietetic treatment; a diet of high caloric value is indicated. The usual site of a subpleural abscess is the convex surface of the lung, in which case a diffuse empyema develops. If the abscess is located in a fissure there will be an interlobar empyema. If it is on the medial aspect of the lung, one or more pockets of pus will form retrosternally between the lung and the mediastinal pleura.

The inflammatory exudate consists mainly of a dense network of fibrin in the meshes of which are serum and large numbers of polymorphonuclear leucocytes. In the course of time the exudate is invaded by fibroblasts which lay down bundles of collagen fibers, so that eventually the affected portion of the lung is covered by a layer of exceedingly dense fibrous tissue, which may attain a remarkable degree of thickness. In some cases it is as much as an inch in depth. A simi-

lar deposit is laid down upon the parietal pleura, and may offer a formidable obstacle to an exploring needle, which should always be of large caliber on account of the ease with which it may be plugged. This thick inflammatory exudate, which may form a capsule for the greater portion of the lung, plays an important part in preventing the subsequent expansion of the lung after the pus has been evacuated. One of the great merits of Dakin's solution of neutral sodium hypochlorite is that it exerts a decorticating action by loosening this deposit and bringing it away in fragments. thus facilitating the expansion of the lung.

Fig. 348.—Empyema with collapse of the lung showing the thick pleural deposit.

One aspect of this deposit of inflammatory material to which attention has only been called recently is the effect produced on the mediastinum. The work of Graham and Bell has revolutionized our conception of the mechanics of the pleural cavities. It used to be considered that each pleural cavity was entirely independent of the other, being separated from it by the firm unyielding partition of the mediastinum, so that if a pneumothorax was produced on one side, although the corresponding lung might collapse, the one on the other side was unaffected. Graham and Bell, however, have shown by their

experimental work on dogs that the mediastinum is a thin mobile partition which offers only a negligible resistance to variations in pressure on either side. A pneumothorax, therefore, will lead to collapse of both lungs, so that if an opening is made in the chest during the acute stage of a streptococcal empyema and pneumonia, the effect on the patient, who already finds difficulty in getting enough air with

FIG. 349.—Empyema with thick fibrinopurulent exudate lining the pleural cavity. Compression and atelectasis of the lung caused by the large amount of fluid which was in the pleural cavity. (MacCallum.)

which to carry on life, may be fatal, as was seen only too well in hundreds of cases during the influenza epidemic.

The deposit of a thick layer of fibrin on the mediastinum with subsequent fibrosis alters all this. A rigid wall is now interposed between the two pleural cavities. A pneumothorax, therefore, will now be entirely one-sided in its effect.

From what has already been said it is evident that even in the early stages of empyema adhesions are formed, which limit the spread of the mischief as much as possible. The analogy to suppuration in the peritoneum again suggests itself. Depending on the site of the infection an abscess may be formed between the convex surface of the lung and the parietes, between the base of the lung and the diaphragm, between the two lobes, or between the lung and the mediastinum. The result is to limit the abscess, so that it is very rare to find the entire pleural cavity filled with pus. This limitation may create great difficulties in diagnosis by means of puncture, for the pus may be so encapsulated, as between two lobes of the lung, that the pocket may be extremely difficult to strike.

The *pus* varies somewhat with the infecting organisms. In pneumococcal cases it is thick, creamy, and yellowish or greenish in color. When due to the streptococcus it is usually, but by no means always, thinner and more watery and contains flakes of fibrin. Tuberculous pus is also thin and contains masses of caseous material. No hard and fast lines can be drawn, however, for on this very day of writing I examined a thick, creamy, and apparently pneumococcal pus which yet contained clumps of tubercle bacilli. The pneumococcus and streptococcus can usually be found in the smears, but it is quite exceptional to find the tubercle bacillus. If the pus has a fecal smell, infection with the colon bacillus may be suspected.

The *effect on the lung* of the purulent exudate is of great importance. The lung is lifted up on the surface of the fluid, and becomes more and more collapsed, until it may form a small compressed mass at the hilus. Moreover a purulent fluid exerts a much more deleterious effect on the lung substance than does a serous collection. There may be necrosis and destruction of the lung tissue at the seat of pressure, together with an interstitial inflammation which results in fibrosis and contraction, and thus still further interferes with subsequent expansion.

Subsequent Course.—If an empyema is left alone it may be recovered from spontaneously provided it is of limited extent. It may kill the patient from septicemia, amyloid disease may develop, or the empyema may rupture externally or into a neighboring cavity such as a bronchus, the esophagus, or the peritoneal cavity. That an empyema may be followed by a metastatic abscess in the brain is well known. Such an abscess, however, must in every case be due to the abscess in the lung which gave rise to the empyema, for there is no conceivable route by which an embolus could pass from the pleural cavity to the brain.

Following an operation the empyema may heal fairly rapidly with expansion of the lung and obliteration of the cavity. Very frequently, however, the condition becomes chronic, pus continues to discharge from the opening for months or it may be years, and the lung refuses to expand. For this there may be a number of reasons, but the two most important are the continuance of the infection and the encapsulation

of the lung by the dense fibrinous deposit. The continuance of the infection is frequently due to the persistance of a pleuro-pulmonary fistula through which fresh infection is continually occurring. It is for this reason that the method of treatment by irrigation with Dakin's solution is often so effective, for the sodium hypochlorite both sterilizes the cavity and decorticates the lung by dissolving the exudate. The greater the chronicity the thicker does the exudate become. In old cases there may be calcification of the thickened pleura.

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CHAPTER XXXVIII

MIDDLE EAR INFLAMMATION

Whilst diseases of the ear come into the domain of the specialist rather than of the general surgeon, inflammation of the middle ear provides a notable exception because at any moment, at any stage of the disease, the inflammation may spread to neighboring vital organs with far-reaching consequences and disastrous effects. The sword of Damocles hangs suspended over the patient by a very thin thread.

Etiology.—The bacteria which are responsible for the inflammation may reach the middle ear: (1) from the external meatus, (2) from the naso-pharynx via the Eustachian tube, or (3) through the blood stream.

The first variety may follow rupture of the tympanic membrane from forcible syringing, the unskilled use of instruments, and fracture of the skull. Any form of external otitis may spread to the middle ear, and foreign bodies and impacted wax may act as exciting causes.

The second variety is predisposed to by any chronic pathological condition of the nose or naso-pharynx of which the most important are adenoids in children and chronic catarrh. Acute infections of the throat such as diphtheria may travel upwards along the Eustachian tube. Clumsy syringing of the nose may force fluids along the same route.

The third variety in which infection is carried by the blood stream occurs in the acute exanthemata, of which scarlet fever, measles, and influenza furnish the most important examples. In these conditions it may be difficult to exclude upward spread from the usually inflamed throat. Tuberculosis of the middle ear is also due to blood spread from some primary focus.

The *bacterial flora* is varied. In acute infections, such as those which complicate scarlet fever and influenza, the streptococcus pyogenes is usually found. A peculiarly viscid or slimy discharge is due to infection with the streptococcus mucosus, an organism which, in spite of its name, is more closely allied to pneumococci than to the streptococci. In exceptional cases the diphtheria bacillus may be present. Those cases due to spread of infection from the throat will usually show the pneumococcus or the streptococcus. When the inflammation has become chronic with discharge through a perforation in the membrane, the staphylococcus, either aureus or albus, replaces the pneumococci and streptococci. In these chronic cases a green or blue color in the pus indicates the presence of Bacillus pyocyaneus. The tubercle bacillus may be found in the discharge. Speaking generally it may be said that in the acute cases the infection is likely to be pure, in the chronic cases it will most probably be mixed.

Pneumococcal infections are most prone to set up mastoid and extra-aural abscesses.

Middle ear inflammation has been subdivided and classified in various ways, but for our present purpose it will be sufficient to recognize two main forms, the catarrhal and the purulent.

Catarrhal otitis media is characterized by swelling and hyperemia of the mucosa lining the tympanum accompanied by a serous or mucoid discharge and not leading to perforation of the tympanic membrane. The inflammatory swelling of the mucosa never reaches an extreme degree, and may entirely subside but inflammation in the middle ear differs from that affecting the mucous membranes of other organs in that there is a great tendency to the formation of very persistent masses of granulation tissue with permanent thickening and adhesions between the tympanic membrane, the ossicles, and the walls of the tympanic cavity, a catarrhal adhesive process of more interest to the otologist than to the general surgeon. The secretion is either quite clear and serous, or viscid and sticky. The inflammation is not severe enough to destroy a portion of the tympanic membrane and thus produce a perforation.

Purulent otitis media differs from the foregoing in the acuteness of the process, in the character of the secretion, and in the involvement of the membrana tympani. The entire mucosa lining the tympanic cavity becomes swollen and intensely hyperemic, and in the most severe cases may display petechial hemorrhages. The submucous connective tissue is infiltrated with inflammatory serum and cells, and in places the surface epithelium may be cast off into the exudate in the cavity. The tympanic membrane soon shows similar changes, becoming extremely congested, covered with an exudate, and completely opaque. The exudate is at first sero-hemorrhagic, but rapidly becomes thick and purulent, with an admixture of flakes of epithelium and red blood cells. In influenzal cases it may be frankly hemorrhagic.

The *course* of the disease is variable. First it may run an acute course in a few days, and then rapidly clear up by draining through the Eustachian tube, in marked distinction to the more chronic catarrhal form of otitis media. Secondly, the inflammatory changes in the tympanic membrane may be so severe that softening and perforation occur. Although in exceptional cases the membrane may give way after a few hours, this accident is usually delayed to the third or fourth day of the attack, and occasionally to the end of the second week. Again, thorough drainage of the middle ear through the perforation may result in rapid recovery with healing of the perforation. Thirdly, the perforation may remain open, with escape through it of the discharge from the chronically inflamed lining membrane. At any moment such a perforation may become obstructed by a mass of inspissated secretion, and the inflammatory fire may flare up again as acutely as ever. In some cases the inflammation subsides and the discharge dries up, the "dry perforation" still remaining open. In chronic inflammatory conditions of the middle ear there is always a

great tendency to the formation of granulomatous masses and mucous polypi.

Complications.—As long as the discharge persists there is the danger of certain complications; at any moment the sword of Damocles may fall. The chief of these complications are: (1) acute mastoiditis, (2) extradural abscess, (3) meningitis, (4) cerebral and cerebellar abscess, and (5) sinus phlebitis. The direction in which the infection spreads from the middle ear will determine which of the complications is likely to occur.

Acute Mastoiditis.—The mastoid antrum, which is merely the posterior end of the tympanic cavity, is early invaded by the purulent secretion from the middle ear. Mastoiditis is most likely to occur in otitis media following influenza and the other infective fevers. In the earlier stages the mastoid cells contain no pus, but the lining mucosa is red and intensely engorged. Later the mastoid cells become filled with pus and granulations, and their walls undergo necrosis as the inflammatory process penetrates beneath the mucous membrane. When an abscess forms in the mastoid process it does so usually in the middle and lower parts, and more especially in the superficial portion lying under the cortical layer.

The inflammation may spread outwards, upwards, or backwards. If *outwards*, a periostitis is set up with the formation of pus on the surface of the mastoid process. The pus may remain in the locality of the mastoid, or it may burrow up under the scalp, or it may pass down to the tip of the mastoid, and, spreading along the digastric groove, give rise to a brawny swelling under the deep fascia of the neck below the mastoid process, a condition known as Bezold's abscess.

If the spread is *upwards* the result will be an extradural abscess, a leptomeningitis, or a cerebral abscess.

Extradural Abscess.—This occurs more frequently as the result of acute than of chronic middle ear suppuration. The pus collects between the dura and the bone in the middle cranial fossa. It may remain remarkably localized for a considerable time, but eventually it will begin to spread. The abscess may communicate with the tympanic cavity by a fistulous opening. In other cases, and these are the more dangerous, no evident communication can be detected; indeed the surface of the bone may be quite intact, the infection having spread upwards along the veins or lymphatics.

Meningitis.—The first indication that the course of an acute otitis media is to be complicated may be the development of meningitis. On the other hand meningitis may be superadded to any of the other complications already enumerated. The infection may spread to the meninges via an ulcerated area in the tegmen tympani, but the more usual course is through the internal auditory meatus from an infected labyrinth. As in the case of extradural abscess there may be no demonstrable path of infection from the tympanic cavity to the meninges. There may be a fistulous opening through the dura, or that membrane may be intact. The pus may spread through the

subarachnoid space to the base of the brain, or upwards over the cerebral hemisphere as far as the convexity, producing a variety of pressure phenomena. The cerebrospinal fluid shows the changes which have been considered in detail in Chapter XXXI.

Serous meningitis is a condition in which there is an aseptic accumulation of cerebrospinal fluid in the subarachnoid space and the cerebral ventricles with the production of pressure symptoms. Apart from middle ear disease the condition is one of great medical importance, especially in children, and is greatly benefited by lumbar puncture. In this place, however, we are only concerned with it as a complication of otitis media. It more frequently accompanies chronic than acute inflammation, and appears to be due rather to the irritating action of absorbed toxins than to the presence of bacteria. It may also accompany extradural abscess, cerebral abscess, or sinus phlebitis. The cerebrospinal fluid is under high pressure, but is quite clear, and contains no inflammatory products.

Brain Abscess.—There are only two common locations of brain abscess secondary to otitis media, namely the temporo-sphenoidal lobe and the hemisphere of the cerebellum on the side of the middle ear disease. The former is more than twice as common as the latter. Abscesses may occur in other parts of the brain, but are very rare, and must be regarded as metastatic in nature.

The path by which the infection has spread from the ear may be very evident. In other cases the bone may appear normal, but microscopic examination will reveal a suppurative infiltration. In still other cases the bone is quite uninvolved, and infection is due to thrombosis and inward spread along a vein.

The characteristics of a temporo-sphenoidal abscess have already been considered in Chapter XXXI, and need not be recapitulated here.

Sinus Phlebitis.—The sinus most frequently involved in middle ear inflammation is naturally the lateral sinus which lies along the inner surface of the mastoid process. From there the inflammation may pass down into the jugular vein with disastrous consequences in the shape of metastic abscesses in the lungs, it may pass to the longitudinal sinus and thus reach the lateral sinus on the other side, or it may spread along the petrosal sinuses to the cavernous sinus. At a recent autopsy on a case of acute otitis media I found all the cranial sinuses with the exception of the superior longitudinal filled with purulent breaking down pus.

The infection first gives rise to a perisinus abscess, with subsequent inflammation of the wall. The infection may pass direct from the bone to the sinus wall, or may be carried by venous channels. It is remarkable, however, that in cases where extensive destruction of the bone has occurred and the wall of the sinus is bathed in pus, there may be no indication of either phlebitis or thrombosis. In such cases the wall is covered by a thick layer of fibrin which evidently provides an efficient protection against further spread of the infection.

The inflammatory changes in the lining of the vessel together with the accompanying thrombosis have already been described in Chapter IX.

Cholesteatoma.—The formation of cholesteatomatous masses in the middle ear is so closely related to the question of suppuration that it may be referred to here. True cholesteatomata are pearly tumors of concentric structures which grow from the brain and the meninges and are probably degenerated endotheliomata. In chronic middle ear inflammation similar firm, white, lamellated masses composed of epithelial cells cornified and shed off from the mucosa are found attached to the lining of the tympanic cavity. These masses may reach a great size and entirely fill the middle ear. They cannot be regarded as true tumors.

A much commoner condition is the formation of soft, friable, cholesteatomatous masses, which make no pretence to arise from the wall of the tympanum. They are composed of masses of shed epithelial cells which have been unable to escape in the discharge owing to insufficient drainage, and which in turn tend to obstruct the perforation in the membrane. Cholesterin crystals may be present in large numbers. Owing to the action of putrefactive bacteria the mass may break down to form a foul-smelling pultaceous material, a condition frequently associated with necrosis and ulceration of the bone and the development of intracranial complications such as cerebral abscess or sinus phlebitis.

Tuberculosis.—Tuberculous inflammation of the middle ear is not so uncommon as used to be supposed. When present it is usually chronic and occurs as a complication of pulmonary tuberculosis. The bacilli reach the middle ear through the Eustachian tube or the lymphatics, rarely by the blood stream. They are only occasionally found in the smears of the discharge.

Varying degrees of destruction may be present. The mucosa may be converted into caseous material. It may be completely ulcerated away, so that the walls of the tympanic cavity are bare. In advanced cases the greater part of the petrous temporal and the mastoid process may be destroyed by caries. Death may be due to tuberculous meningitis or brain abscess.

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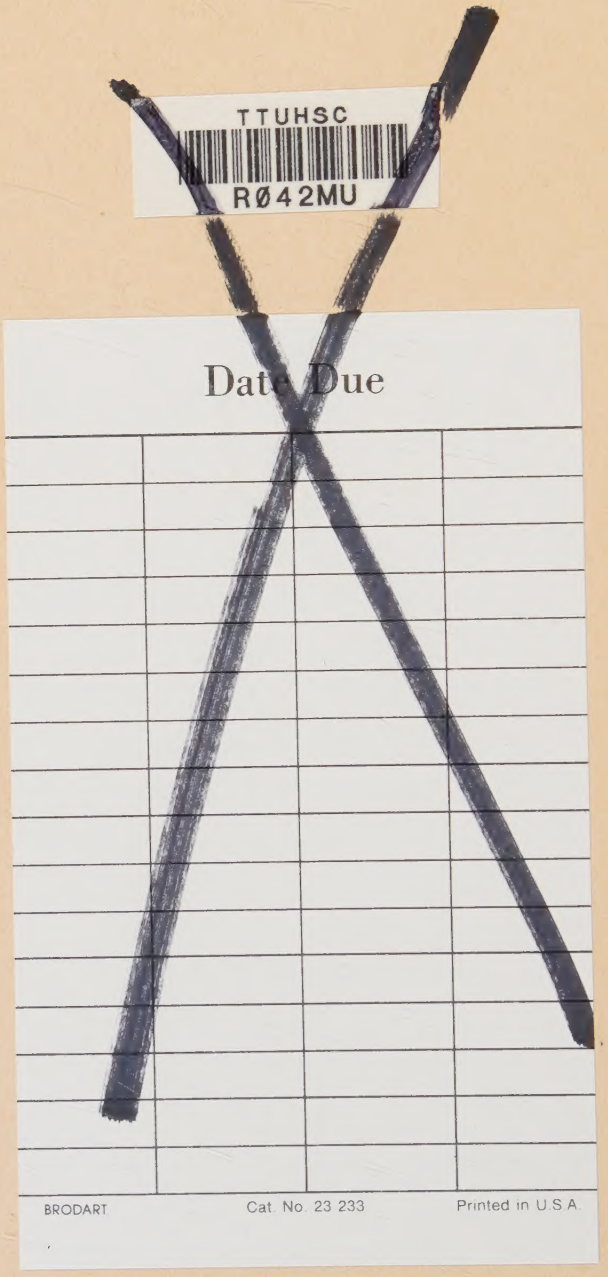
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